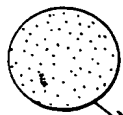


FIG. 1

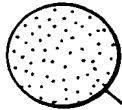


[SEQ. ID NO: 3]

X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C
5' 3'

G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X
3' 5'

[SEQ. ID NO: 4]



X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C

G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X

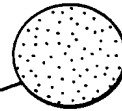


FIG. 2

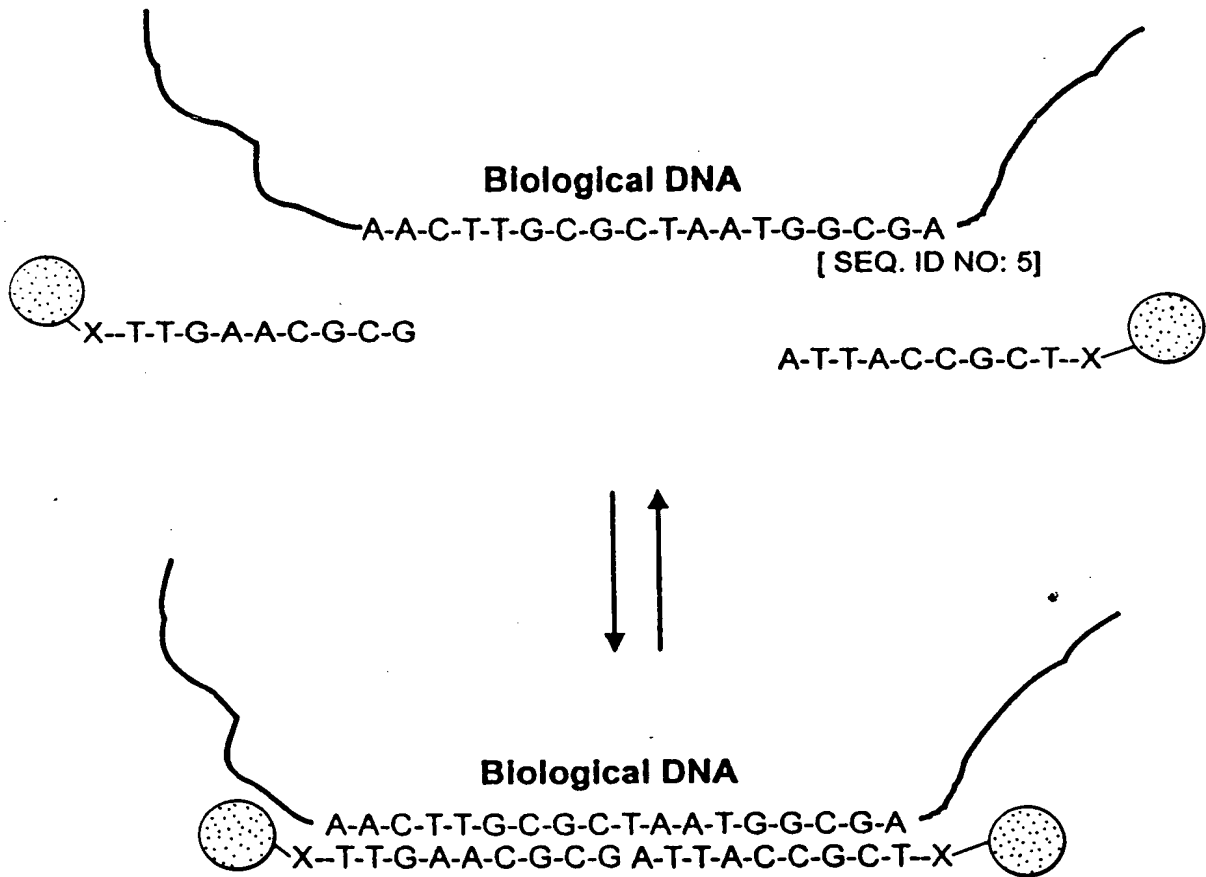


FIG. 4 5' A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G 3' Linking oligonucleotide
 [SEQ. ID NO: 2] A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A 5' [SEQ. ID NO: 1]

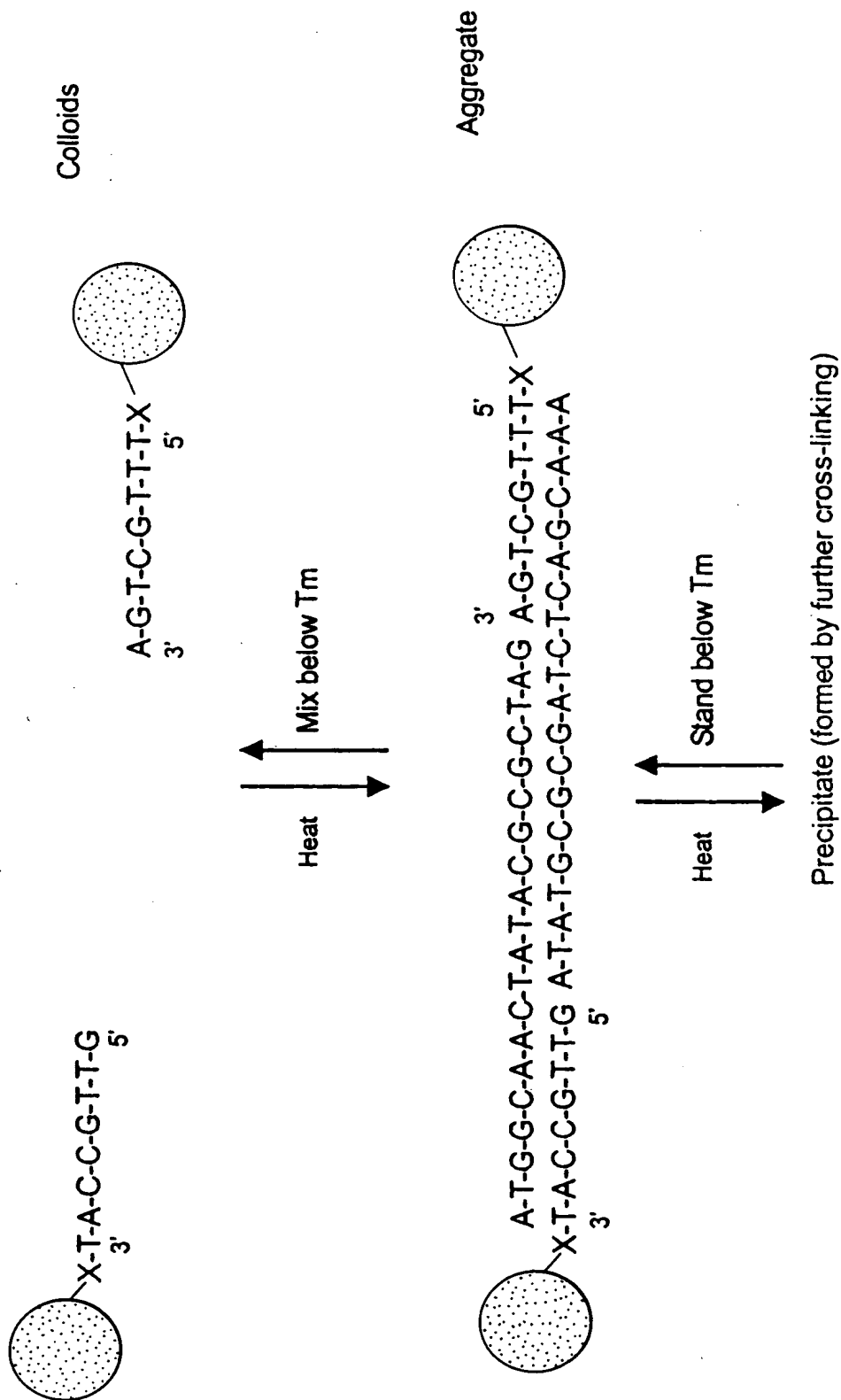
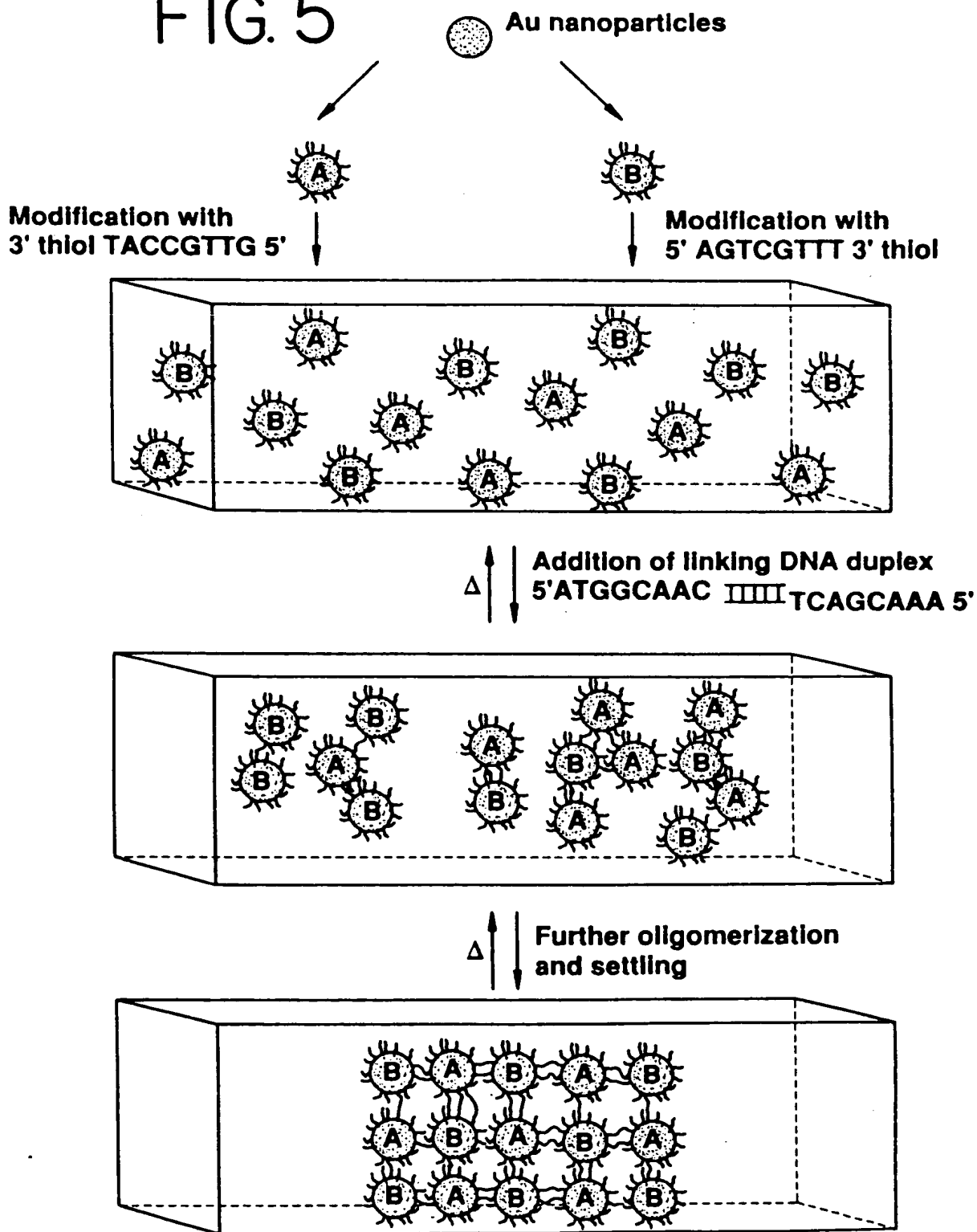
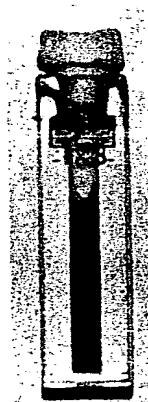


FIG. 5



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FOOTER 2/2660



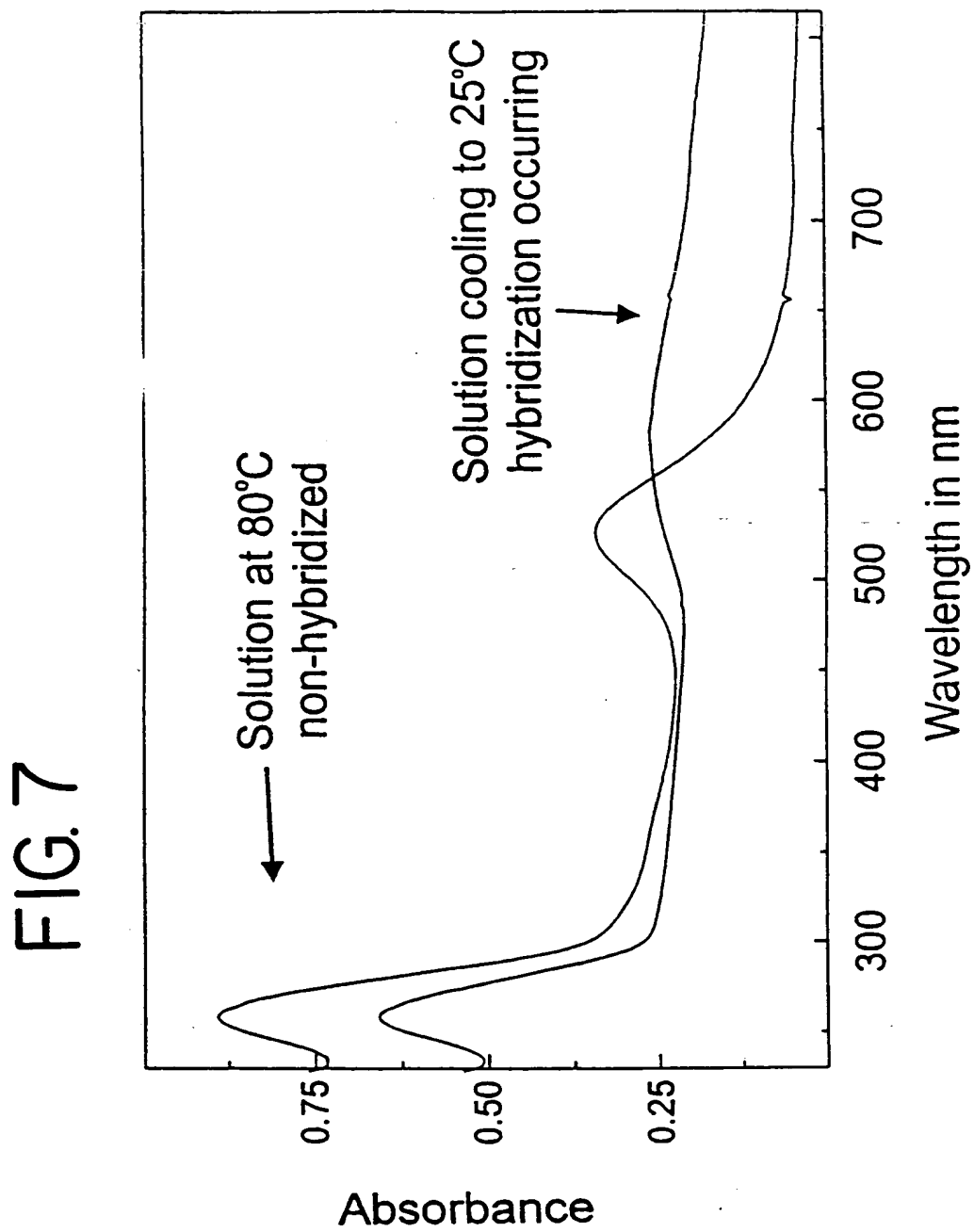


FIG. 8B

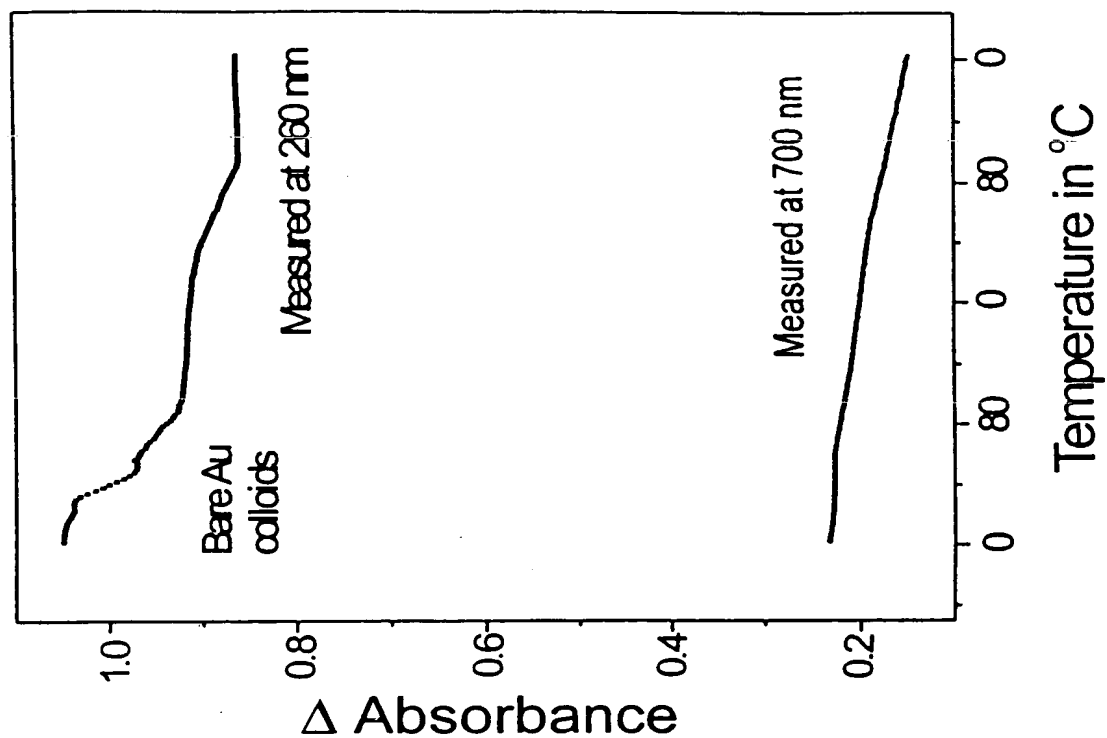
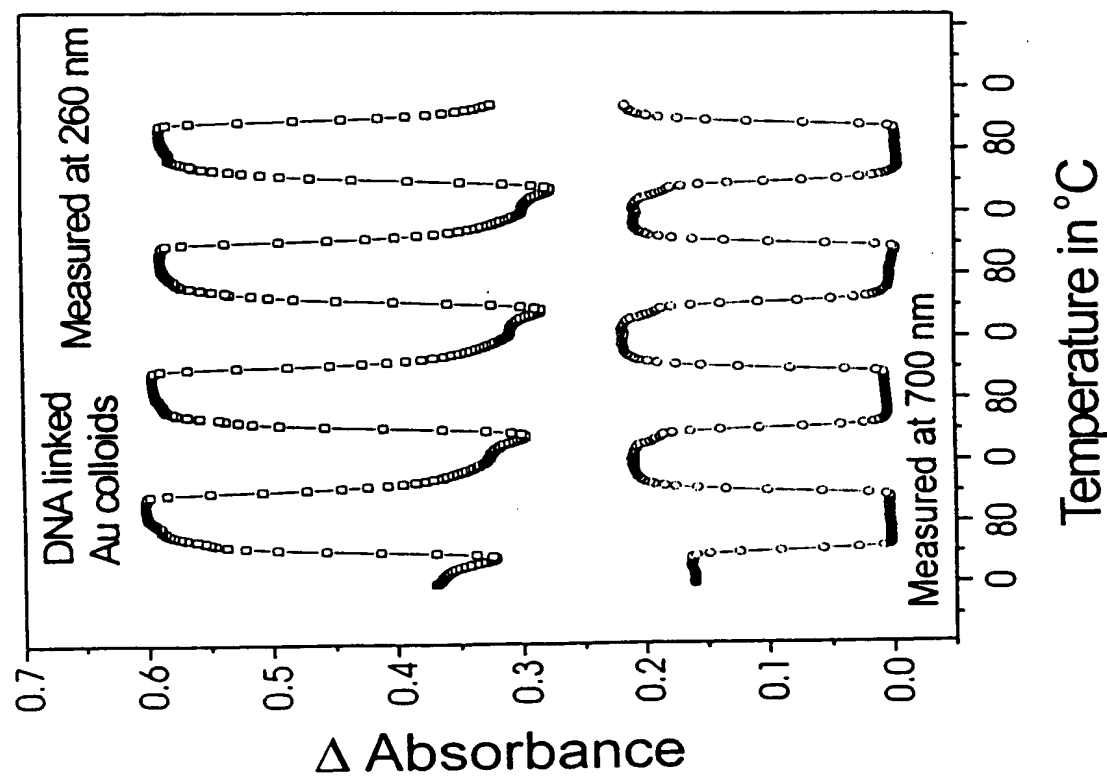


FIG. 8A



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FIG. 9A

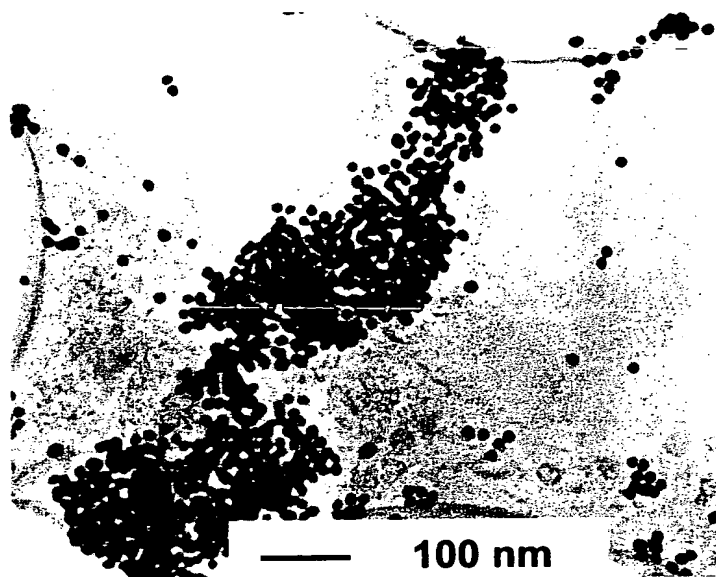
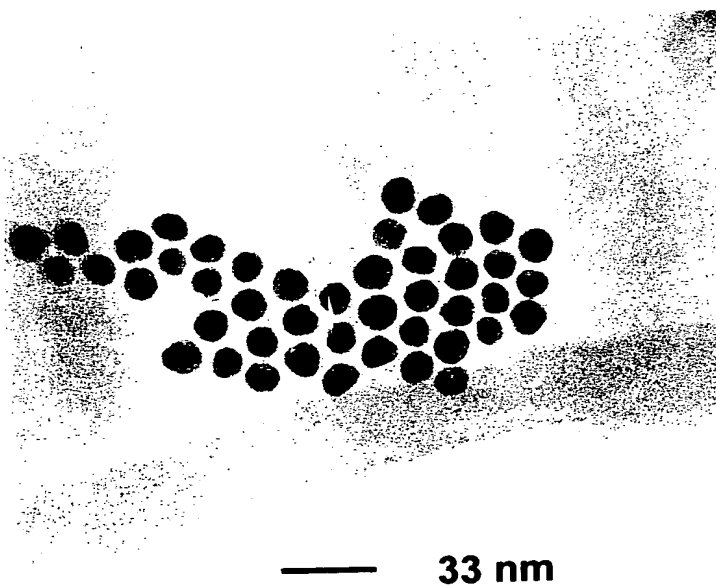


FIG. 9B



0992777-081001

FIG. 10

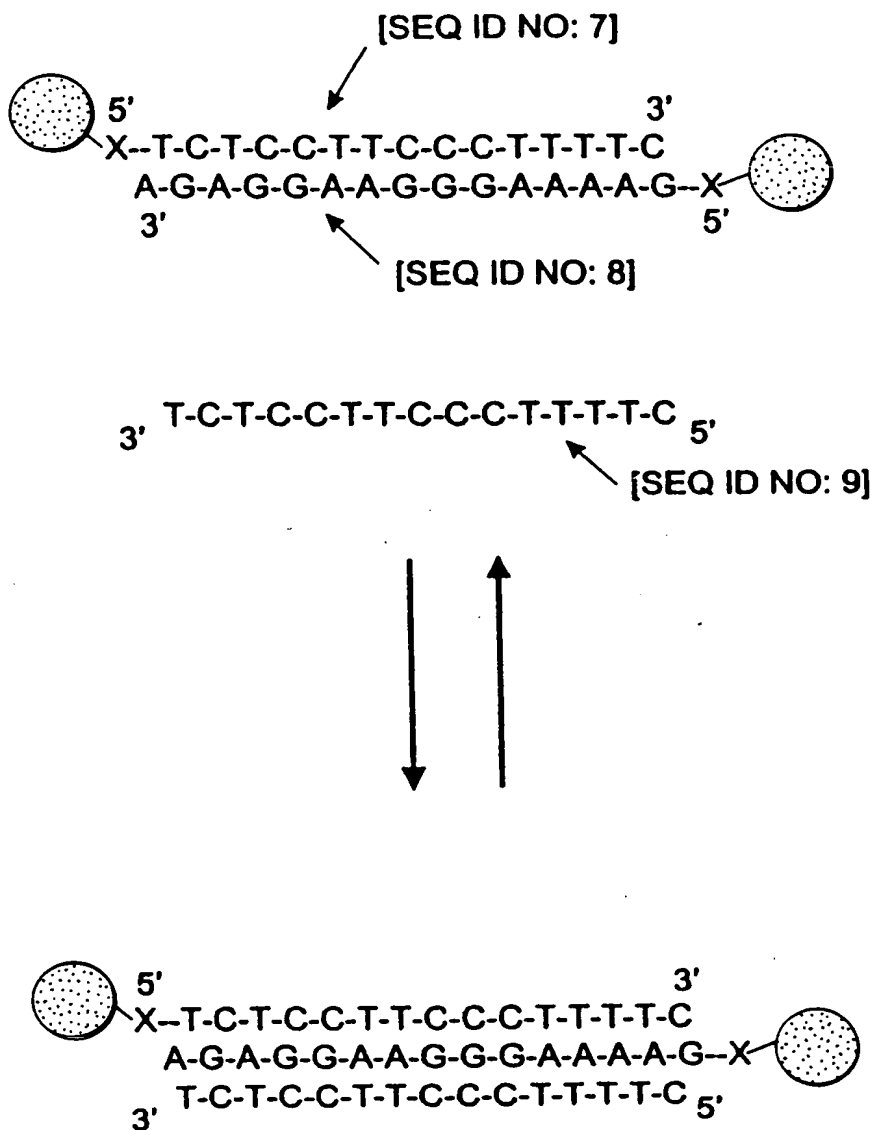
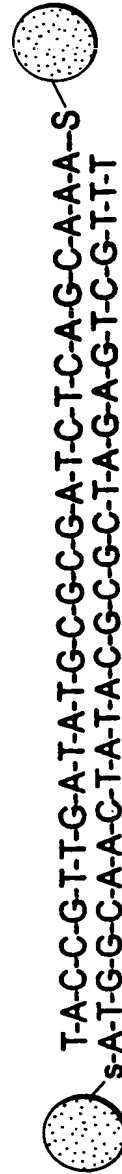
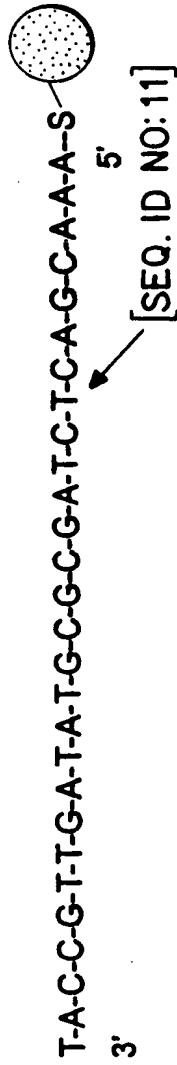
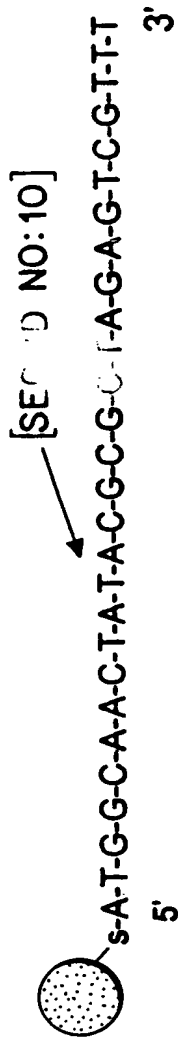


FIG. II



Complementary Target

1

2

3

Probes without Target

1

2

FIG. 12C

1

2

4

FIG. 12D

1

2

5

FIG. 12E

1

2

6

FIG. 12F

1

2

7

[SEQ. ID NO: 18]

Year	Age	Sex	Weight (kg)	Length (cm)	Condition
1971	1	M	1.2	15	Good
1972	2	F	1.5	18	Good
1973	3	M	1.8	20	Good
1974	4	F	2.1	22	Good
1975	5	M	2.4	24	Good
1976	6	F	2.7	26	Good
1977	7	M	3.0	28	Good
1978	8	F	3.3	30	Good
1979	9	M	3.6	32	Good
1980	10	F	3.9	34	Good
1981	11	M	4.2	36	Good
1982	12	F	4.5	38	Good
1983	13	M	4.8	40	Good
1984	14	F	5.1	42	Good
1985	15	M	5.4	44	Good
1986	16	F	5.7	46	Good
1987	17	M	6.0	48	Good
1988	18	F	6.3	50	Good
1989	19	M	6.6	52	Good
1990	20	F	6.9	54	Good
1991	21	M	7.2	56	Good
1992	22	F	7.5	58	Good
1993	23	M	7.8	60	Good
1994	24	F	8.1	62	Good
1995	25	M	8.4	64	Good
1996	26	F	8.7	66	Good
1997	27	M	9.0	68	Good
1998	28	F	9.3	70	Good
1999	29	M	9.6	72	Good
2000	30	F	9.9	74	Good
2001	31	M	10.2	76	Good
2002	32	F	10.5	78	Good
2003	33	M	10.8	80	Good
2004	34	F	11.1	82	Good
2005	35	M	11.4	84	Good
2006	36	F	11.7	86	Good
2007	37	M	12.0	88	Good
2008	38	F	12.3	90	Good
2009	39	M	12.6	92	Good
2010	40	F	12.9	94	Good
2011	41	M	13.2	96	Good
2012	42	F	13.5	98	Good
2013	43	M	13.8	100	Good
2014	44	F	14.1	102	Good
2015	45	M	14.4	104	Good
2016	46	F	14.7	106	Good
2017	47	M	15.0	108	Good
2018	48	F	15.3	110	Good
2019	49	M	15.6	112	Good
2020	50	F	15.9	114	Good
2021	51	M	16.2	116	Good
2022	52	F	16.5	118	Good
2023	53	M	16.8	120	Good
2024	54	F	17.1	122	Good
2025	55	M	17.4	124	Good
2026	56	F	17.7	126	Good
2027	57	M	18.0	128	Good
2028	58	F	18.3	130	Good
2029	59	M	18.6	132	Good
2030	60	F	18.9	134	Good
2031	61	M	19.2	136	Good
2032	62	F	19.5	138	Good
2033	63	M	19.8	140	Good
2034	64	F	20.1	142	Good
2035	65	M	20.4	144	Good
2036	66	F	20.7	146	Good
2037	67	M	21.0	148	Good
2038	68	F	21.3	150	Good
2039	69	M	21.6	152	Good
2040	70	F	21.9	154	Good
2041	71	M	22.2	156	Good
2042	72	F	22.5	158	Good

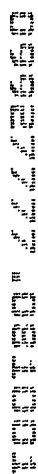


FIG. 13B

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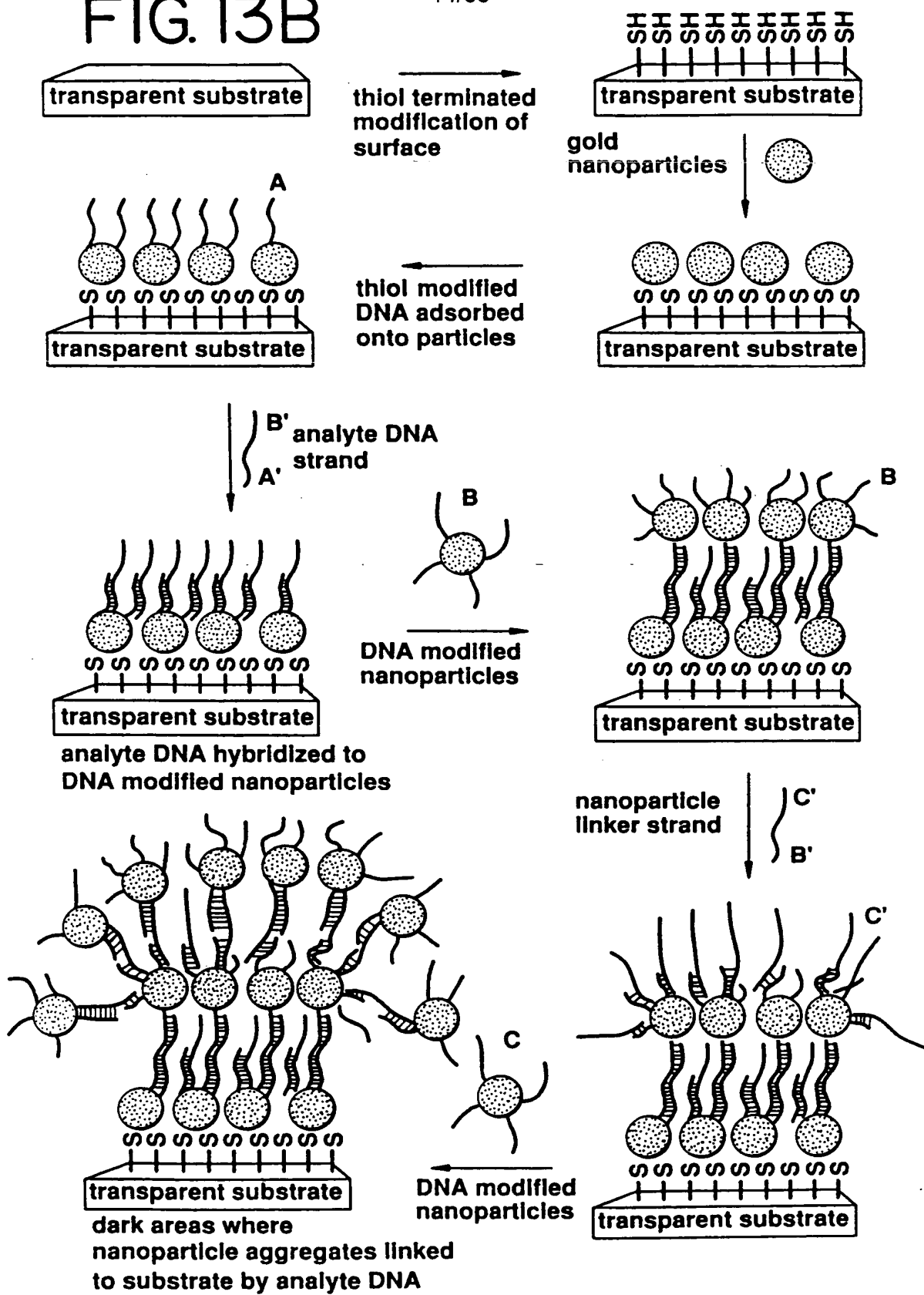


FIG. 14A

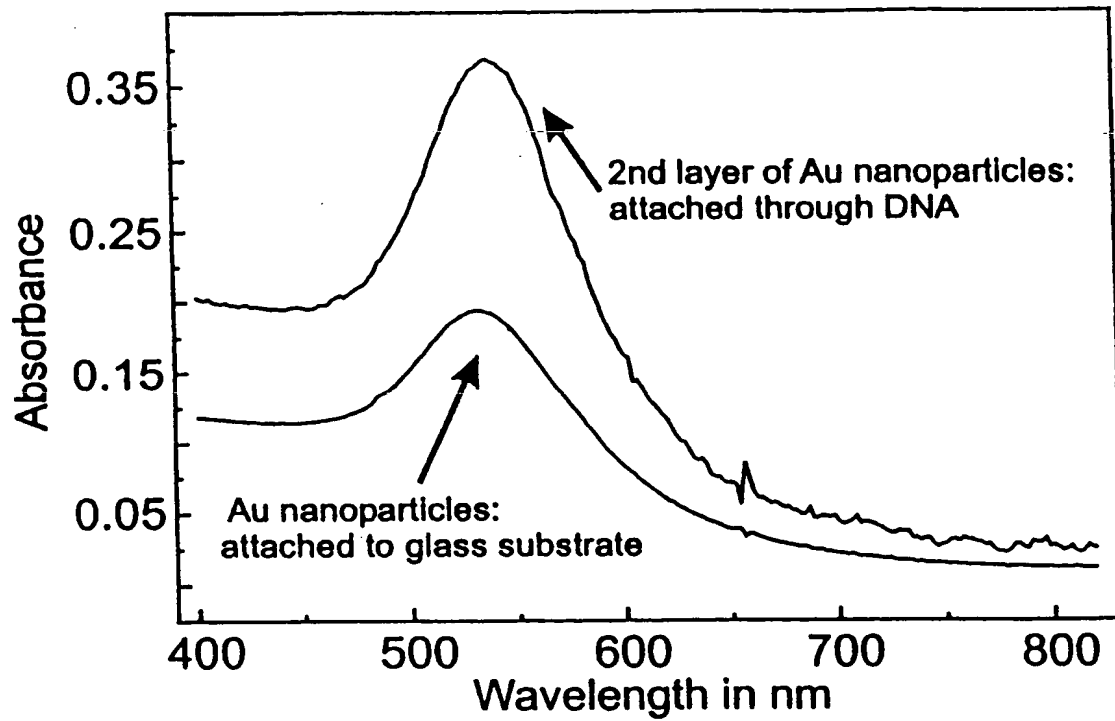


FIG. 14B

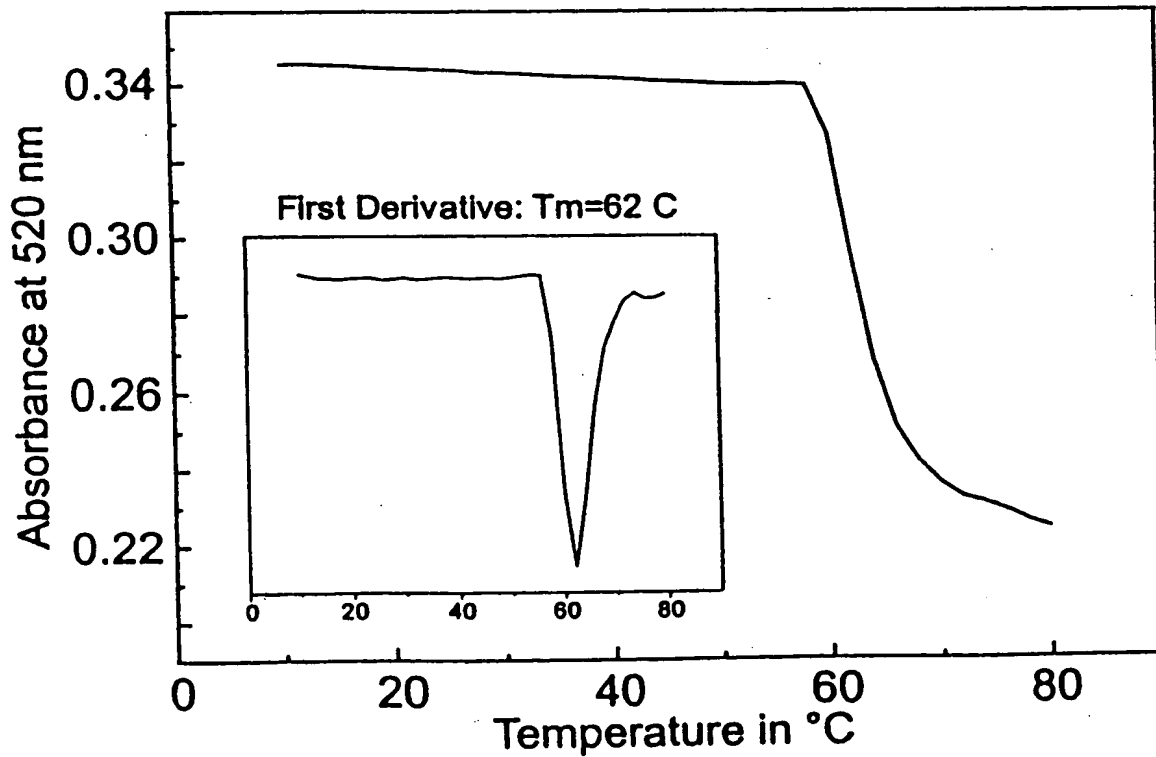


FIG. 15A

Probes with No Target

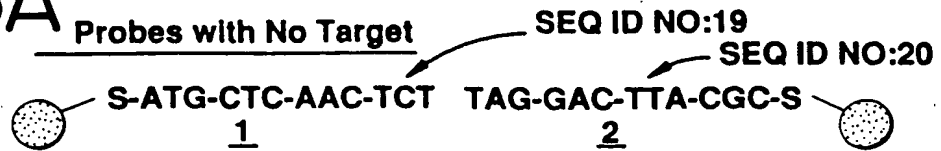


FIG. 15B

Half-Complementary Target

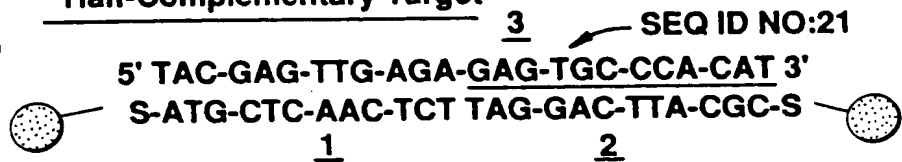


FIG. 15C

Complementary Target

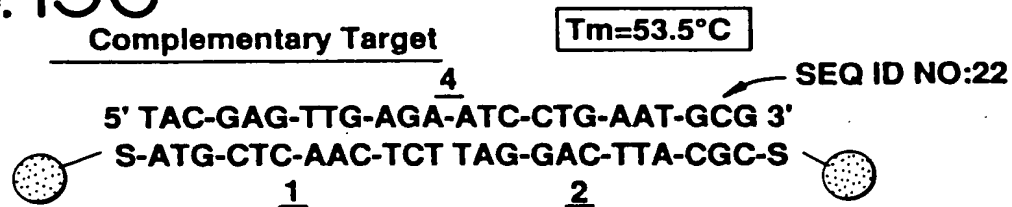


FIG. 15D

ONE Base-Pair Mismatch at Probe Head

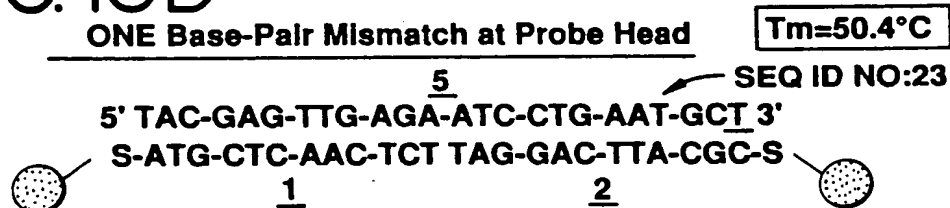


FIG. 15E

ONE Base-Pair Mismatch at Probe Tail

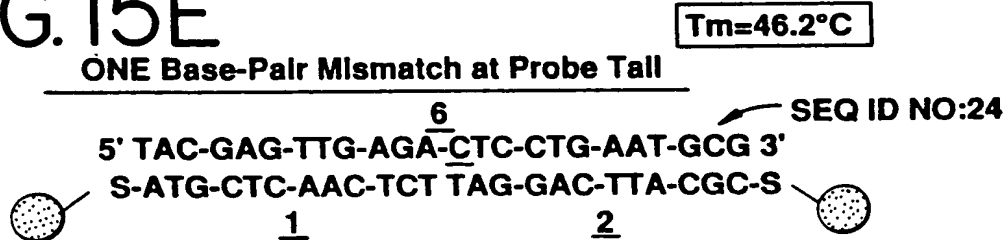


FIG. 15F

ONE Base Deletion

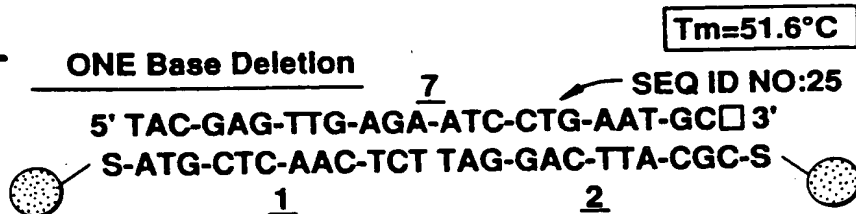
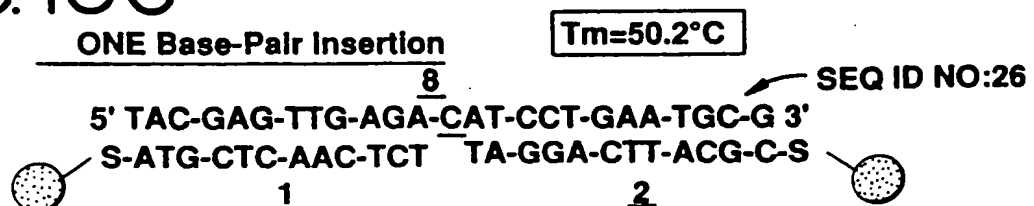


FIG. 15G

ONE Base-Pair Insertion



24 Base Template

FIG. 16A

5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GCG 3'
 —S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S —
 1 2

FIG. 16B

48 Base Template with Complementary 24 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-ATC-CTG-AAT-GCG 3'
 —S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT TAG-GAC-TTA-CGC-S —
 1 2

FIG. 16C

72 Base Template with Complementary 48 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-TAT-ATT-GGA-CGC-TTT-ACG-GAC-AAC-ATC-CTG-AAT-GCG 3'
 —S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT-ATA-TAA-CCT-GCG-AAA-TGC-CTG-TTG TAG-GAC-TTA-CGC-S —
 1 2

FIG. 17A

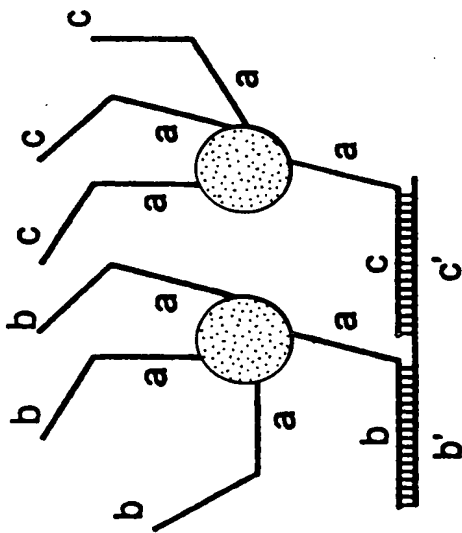


FIG. 17B

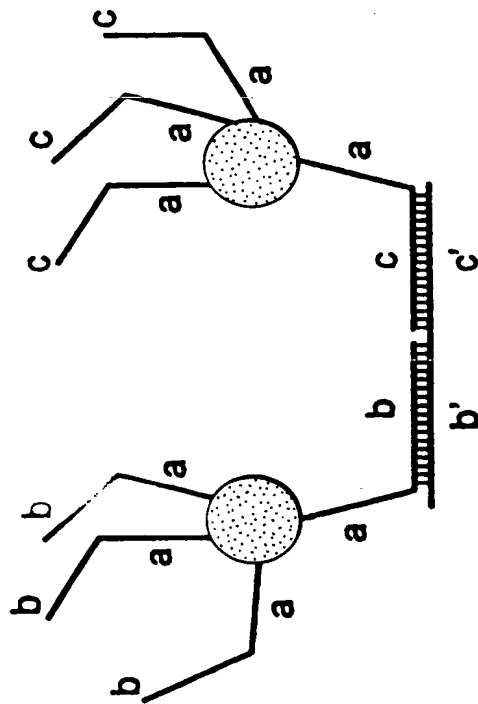


FIG. 17C

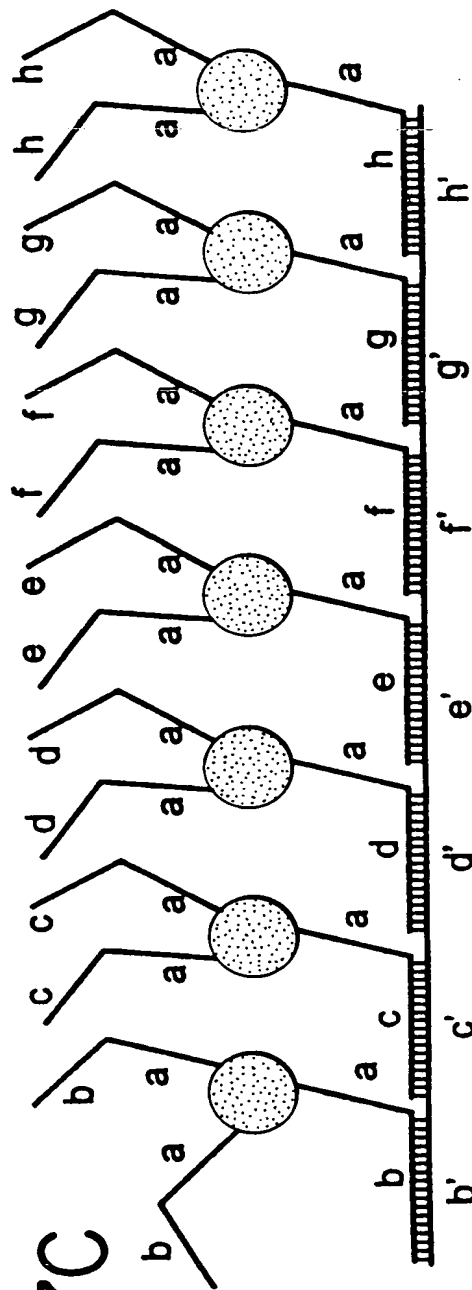


FIG. 17D

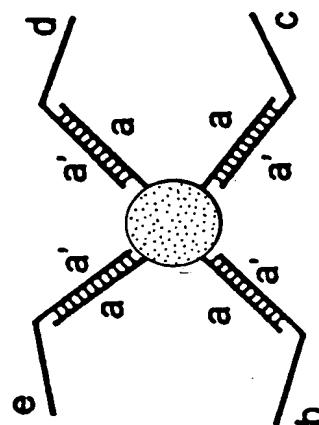
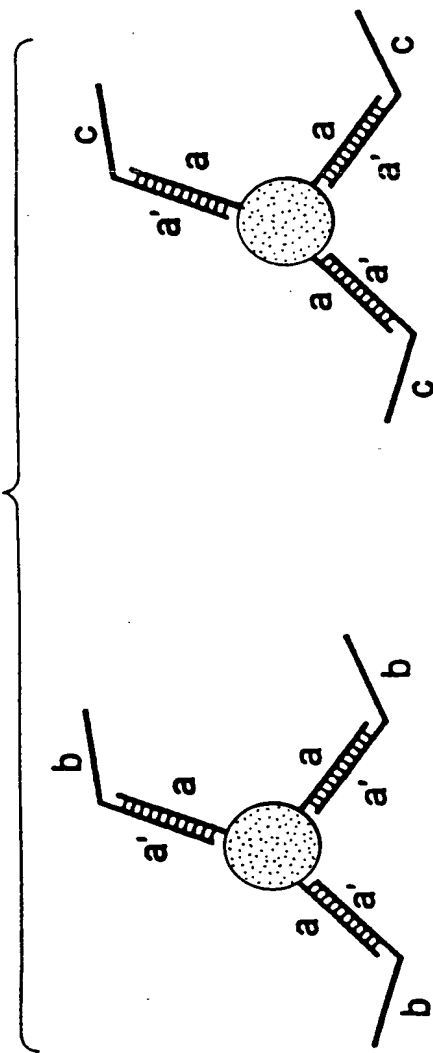


FIG. 17E

FIG. 18

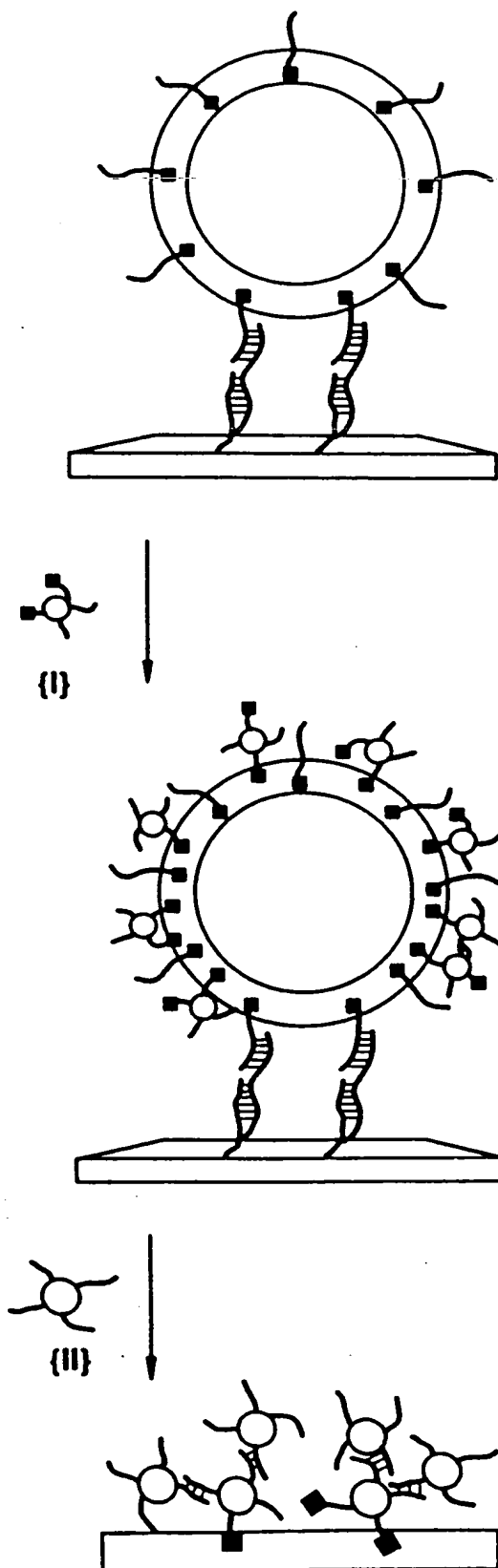


FIG. 19A

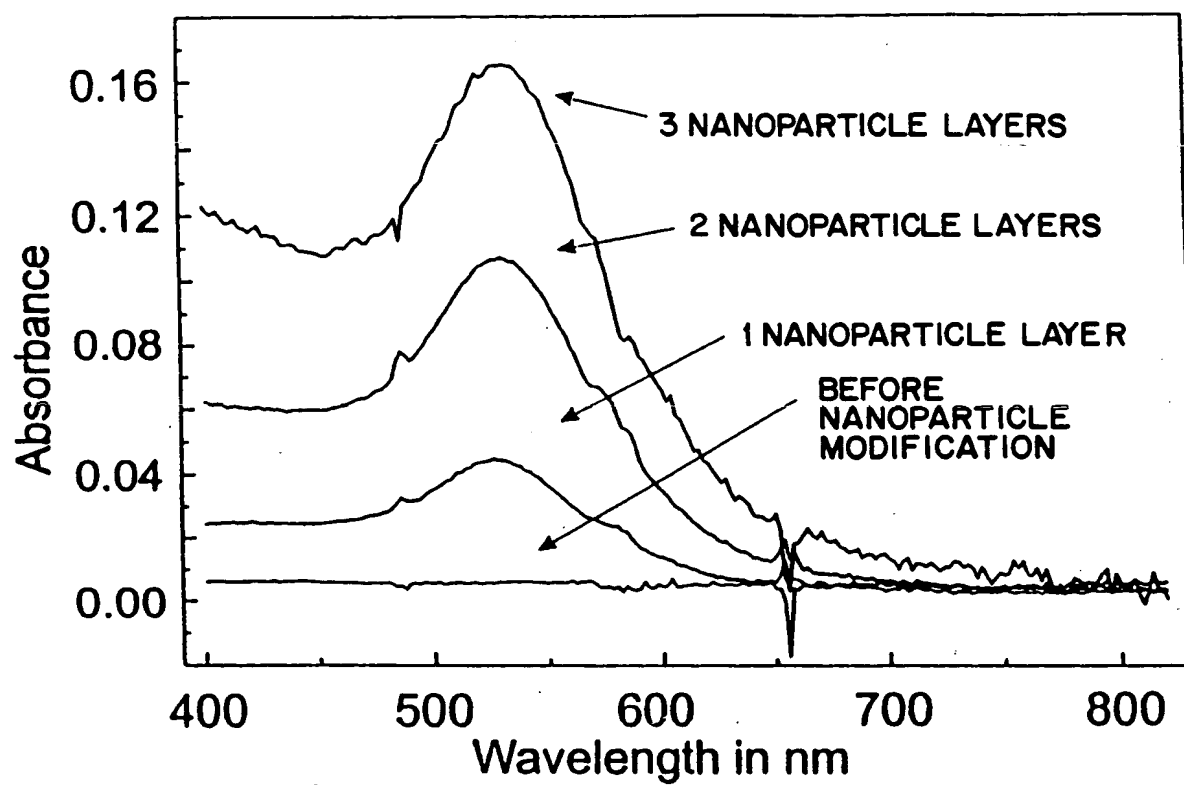
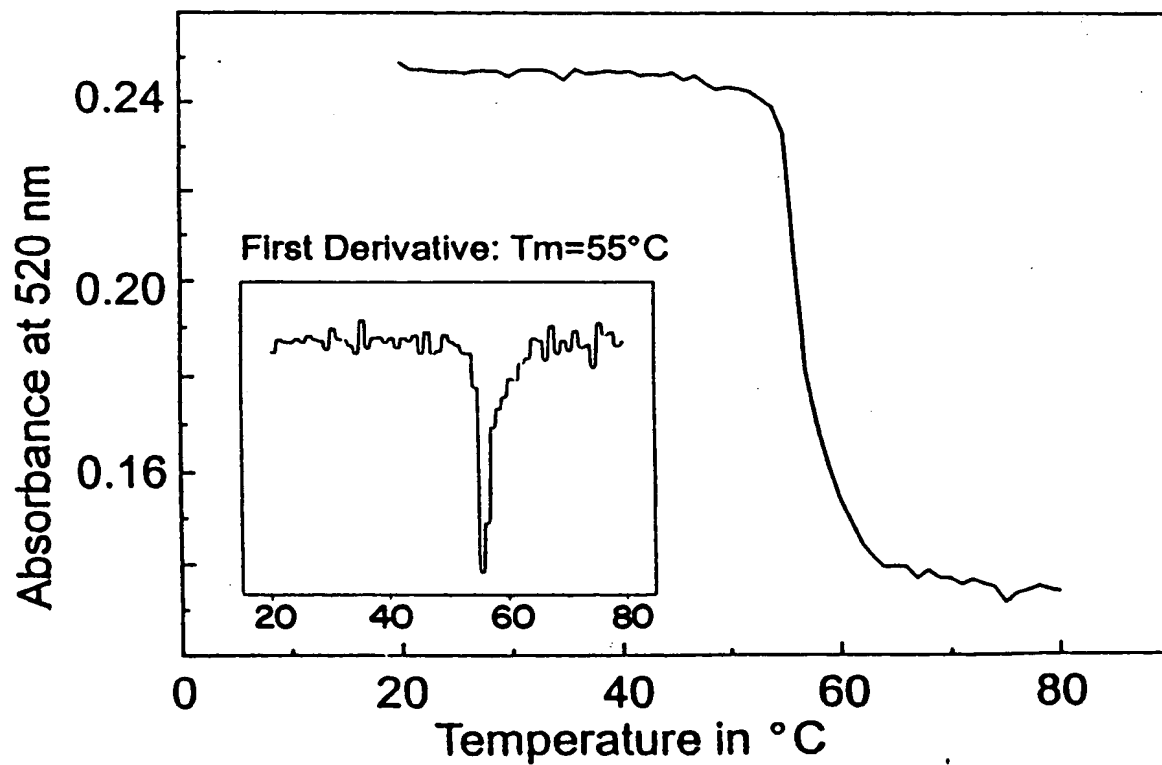


FIG. 19B



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FIG. 20A

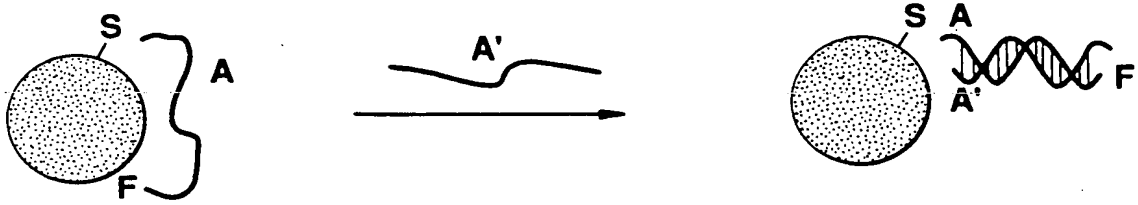


FIG. 20B

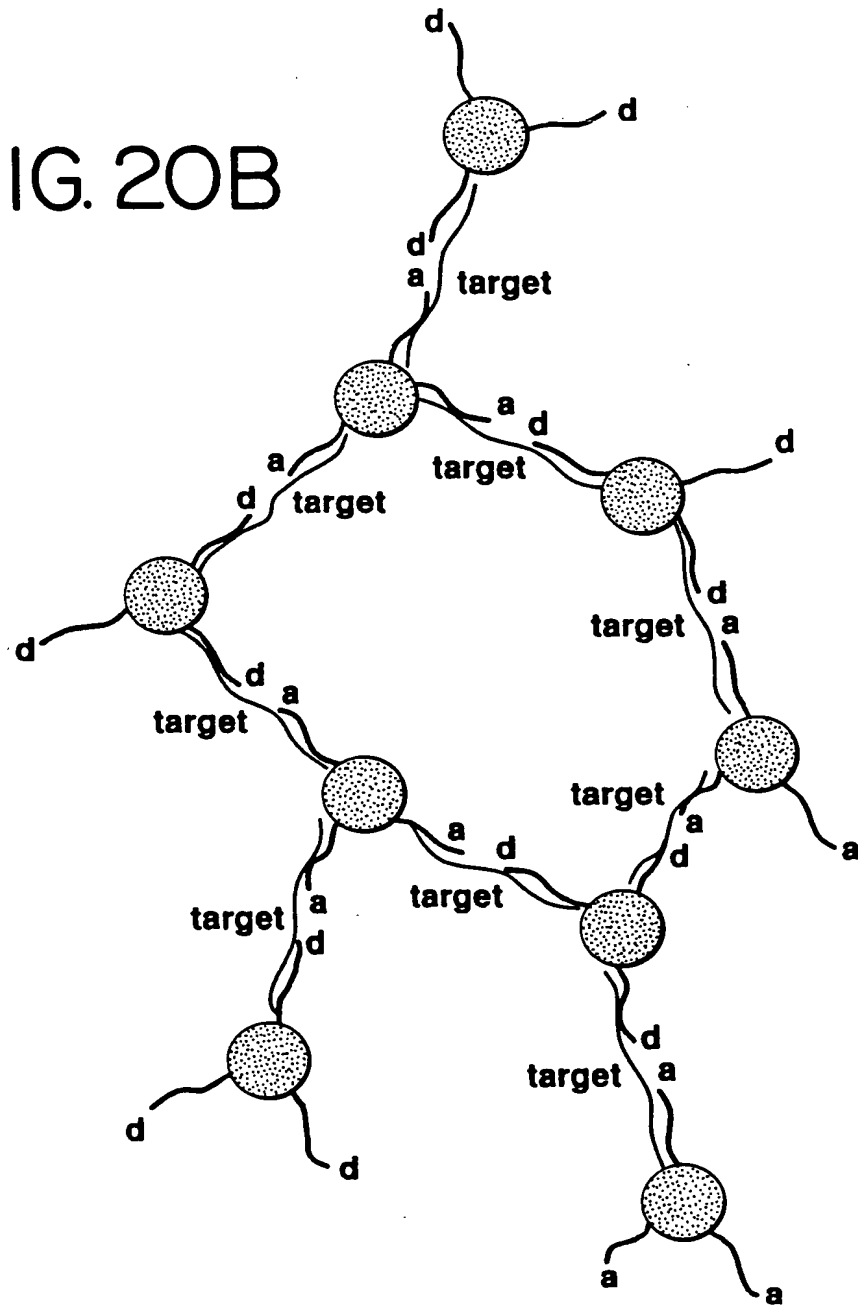


FIG. 20B

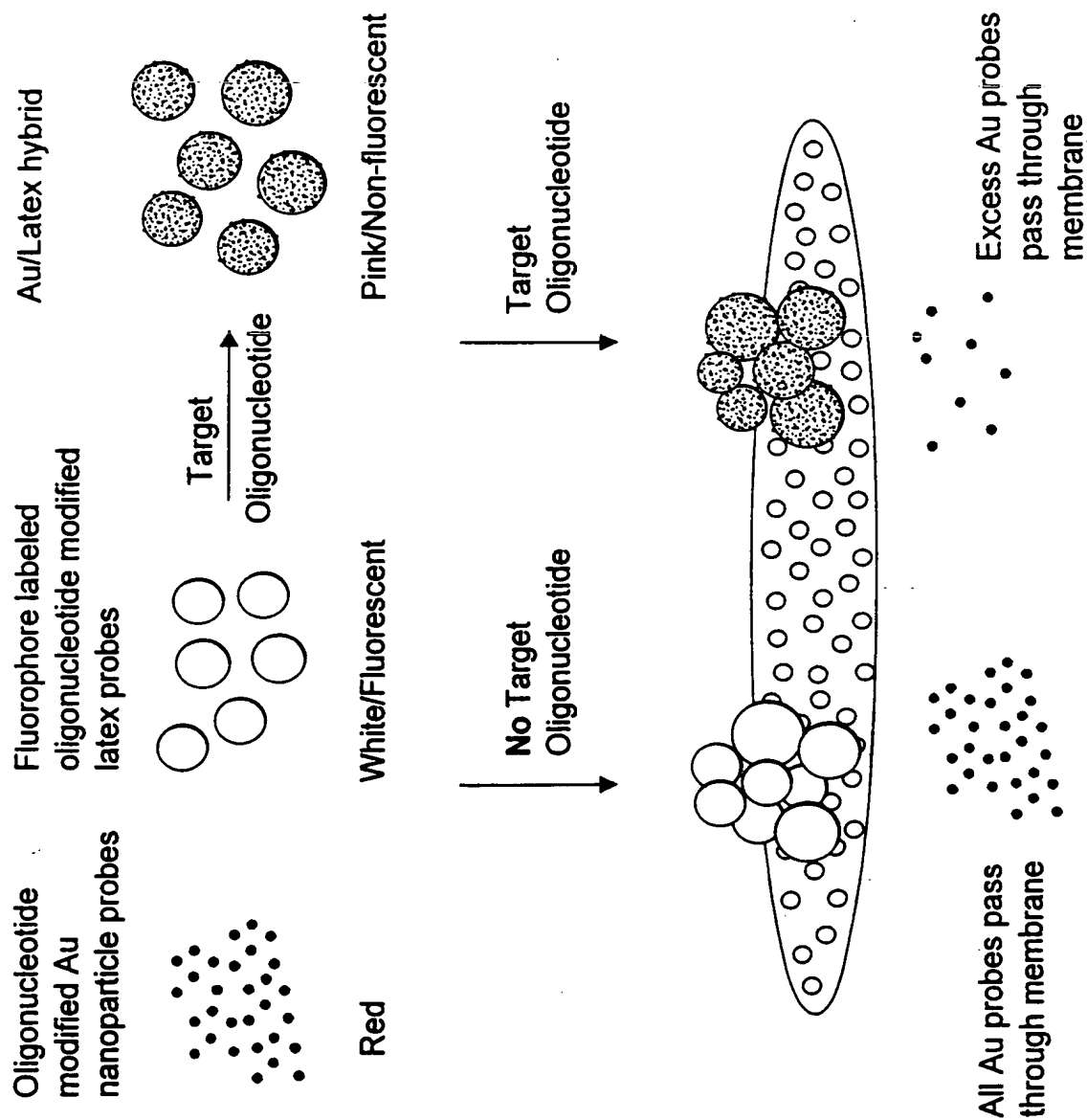
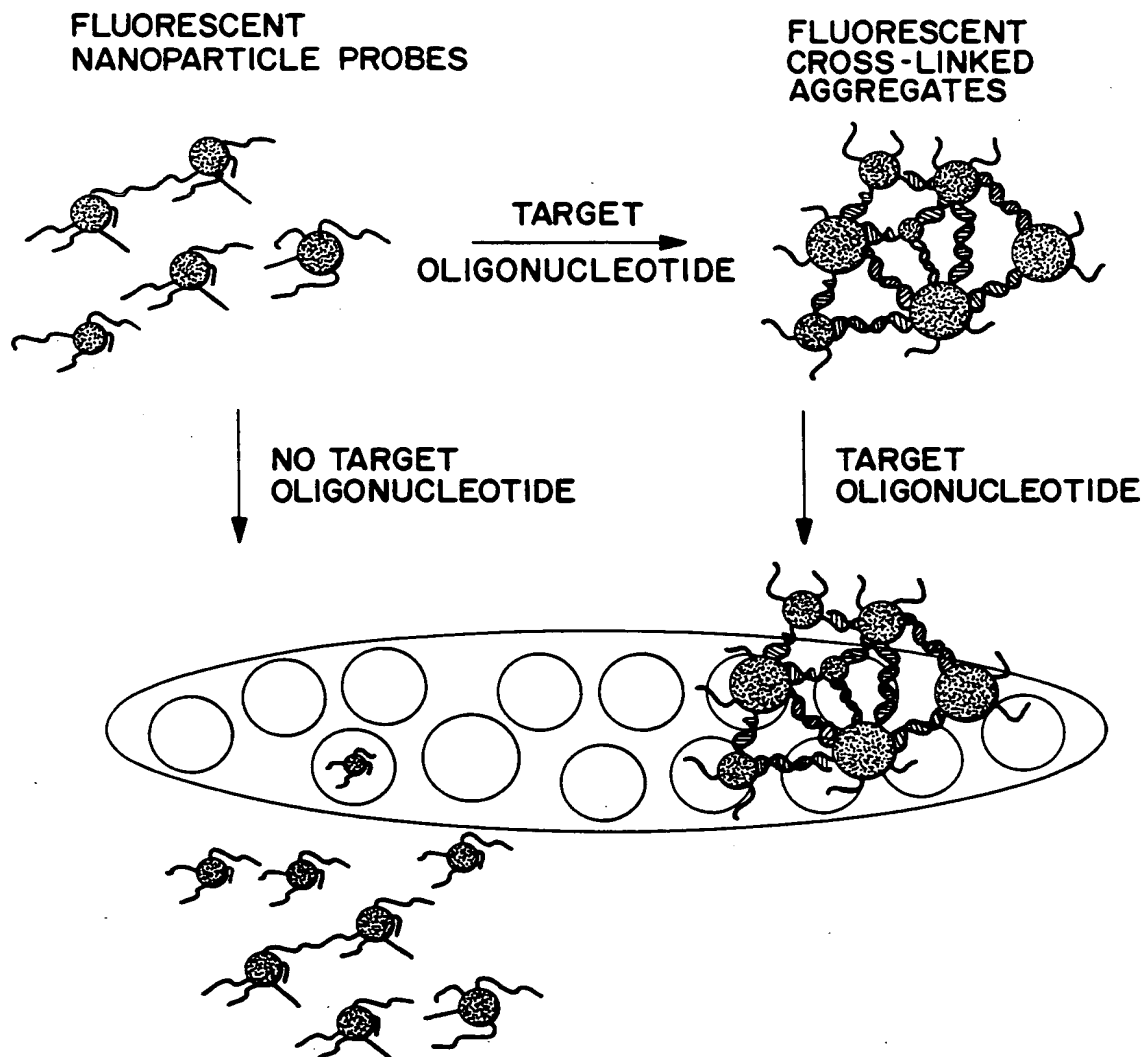


FIG. 22



**THE FLUORESCENT NANOPARTICLE
PROBES PASS THROUGH THE
MEMBRANE**

**THE FLUORESCENT
CROSS-LINKED AGGREGATES
ARE RETAINED BY THE
MEMBRANE**

FIG. 23

Anthrax PCR Product

5'G GCG GAT GAG TCA GTA GTT AAG GAG GCT CAT AGA GAA GTA ATT AAT
3'C CGC CTA CTC AGT CAT CAA TTC CTC CGA GTA TCT CTT CAT TAA TTA

TCG TCA ACA GAG GGA TTA TTG TTA AAT ATT GAT AAG GAT ATA AGA AAA
AGC AGT TGT CTC CCT AAT AAC AAT TTA TAA CTA TTC CTA TAT TCT TTT

ATA TTA TCC AGG GTT ATA TTG TAG AAA TTG AAG ATA CTG AAG GGC TT 3'
TAT AAT AGG TCC CAA TAT AAC ATC TTT AAC TTC TAT GAC TTC CCG AA 5'

141 mer Anthrax PCR product [SEQ ID NO:36]

3' CTC CCT AAT AAC AAT — 

[SEQ ID NO:37]

3' TTA TAA CTA TTC CTA — 

[SEQ ID NO:38]

Oligonucleotide-Nanoparticle Probes

Blocker Oligonucleotides

3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GT

[SEQ ID NO:39]

3' A TCT CTT CAT TAA TTA AGC AGT TGT

[SEQ ID NO:40]

3' TAT TCT TTT TAT AAT AGG TCC CAA TAT

[SEQ ID NO:41]

3' AAC ATC TTT AAC TTC TAT GAC TTC CCG AA

[SEQ ID NO:42]

FIG. 24

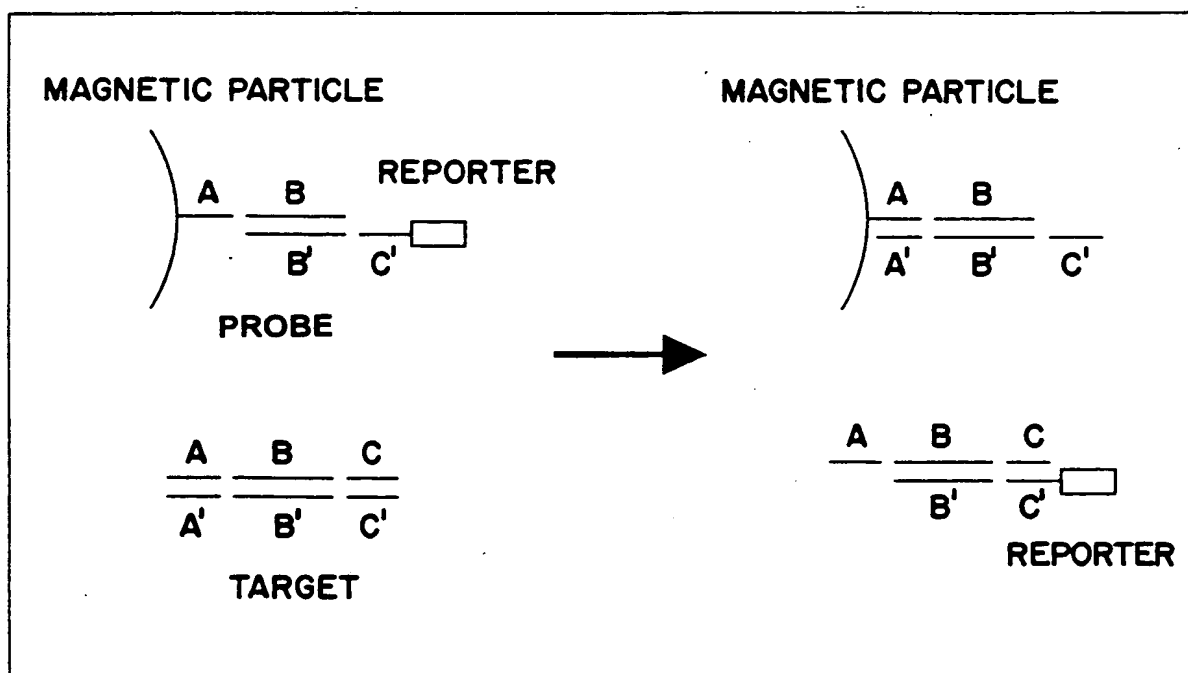
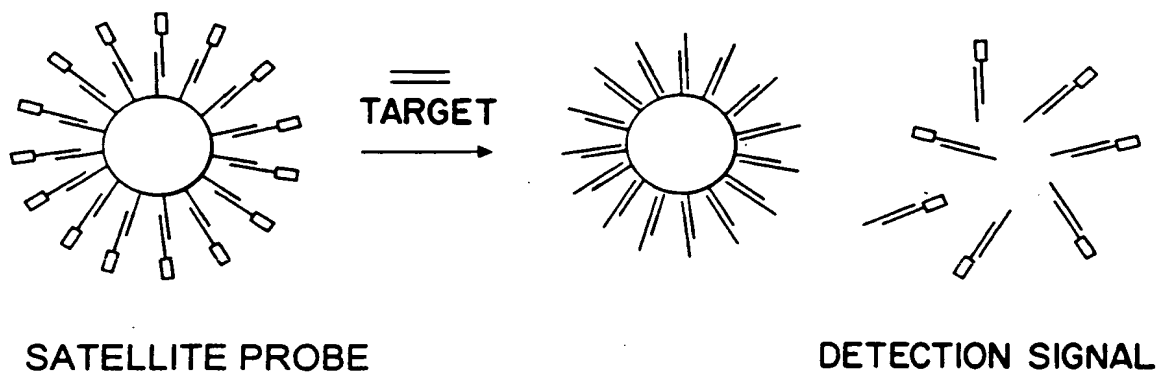


FIG. 25A

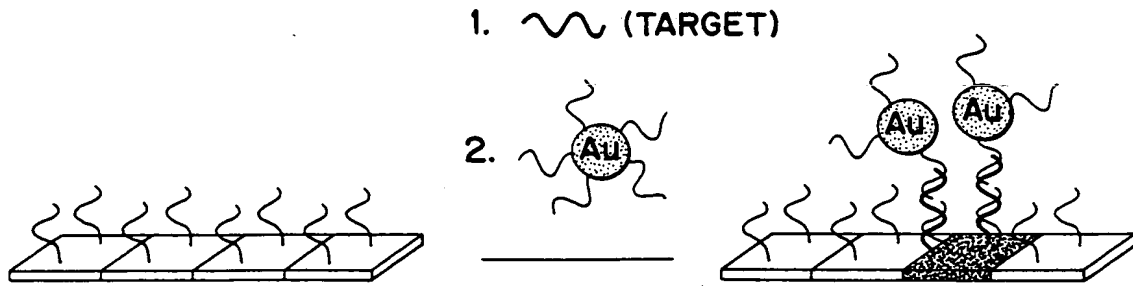


FIG. 25B

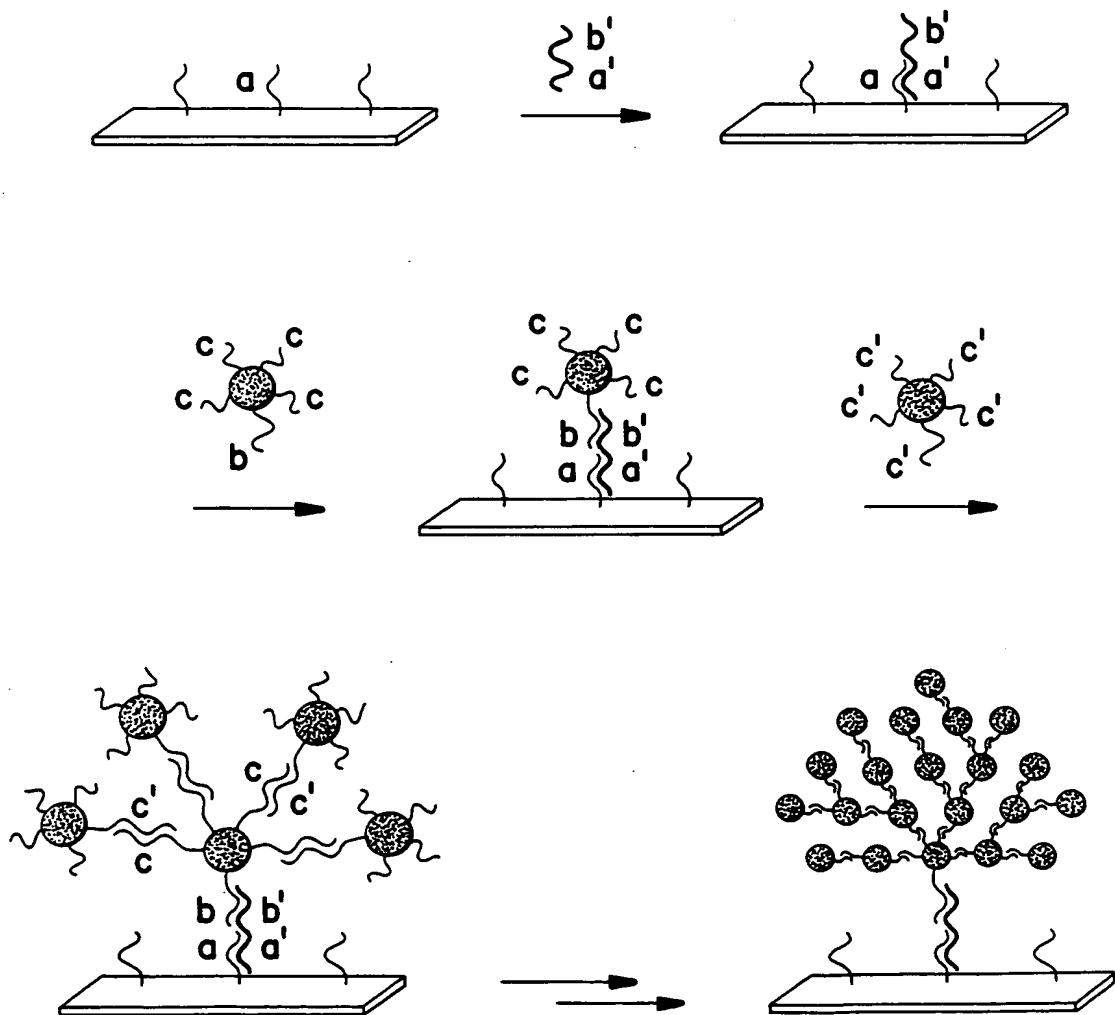


FIG. 26A

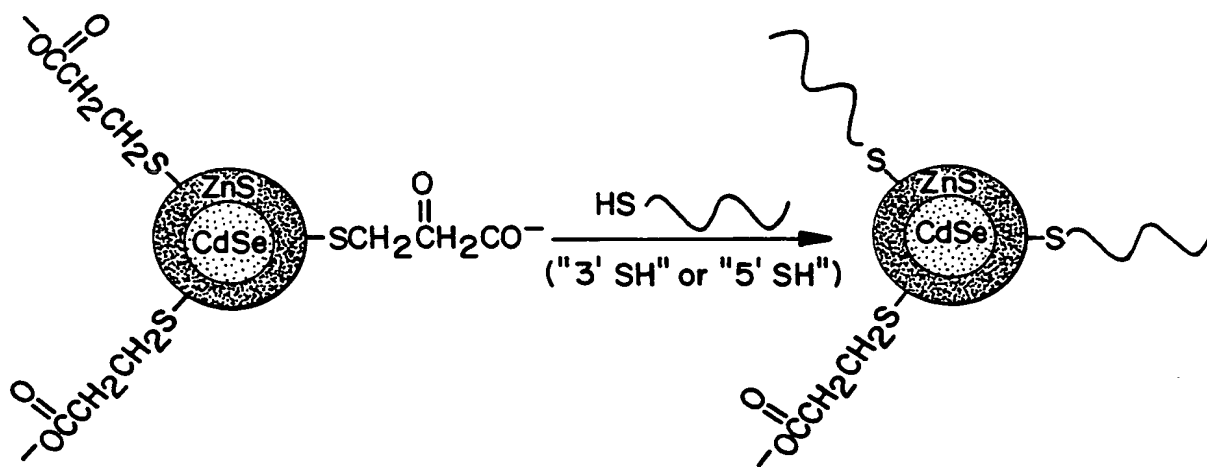


FIG. 26B

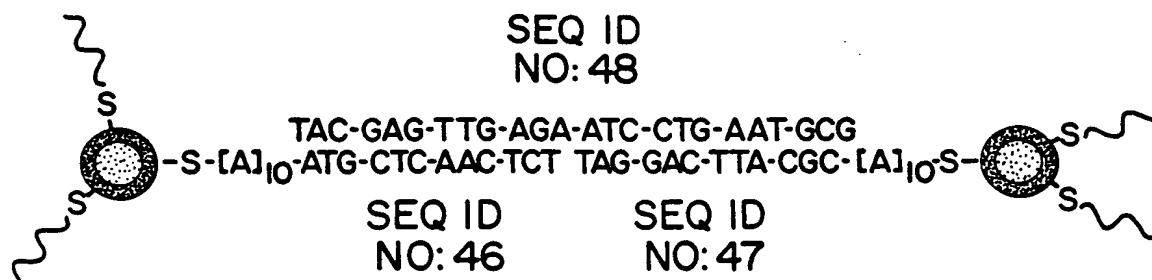


FIG. 27A

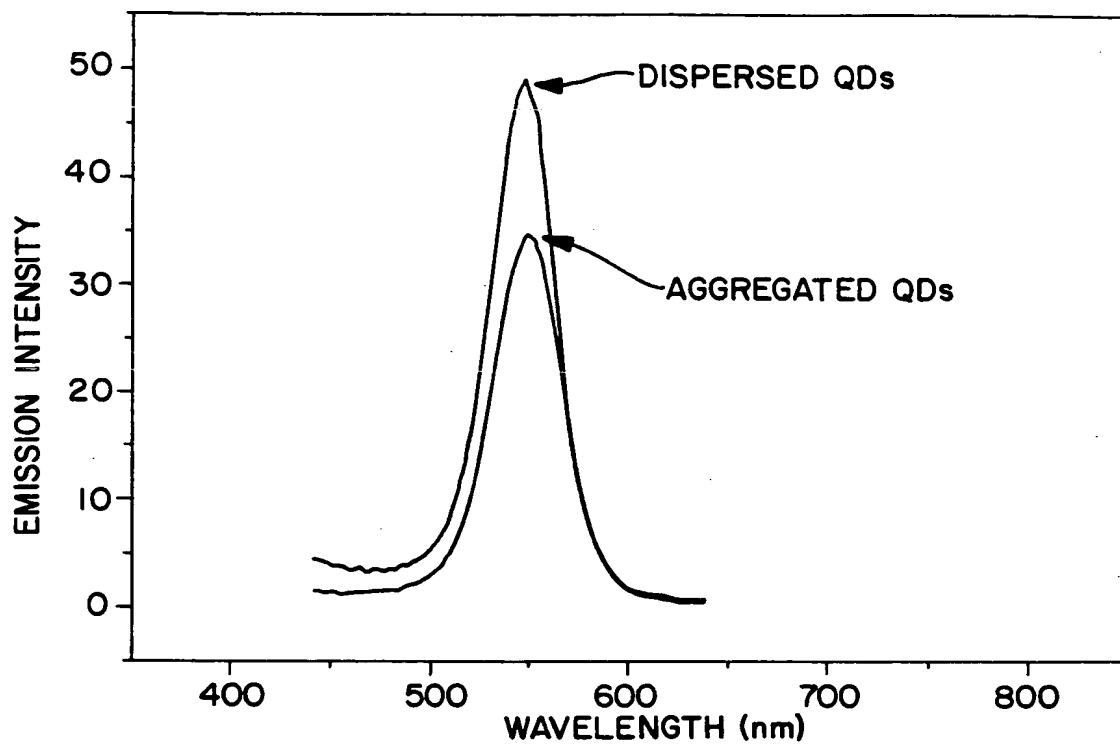


FIG. 27B

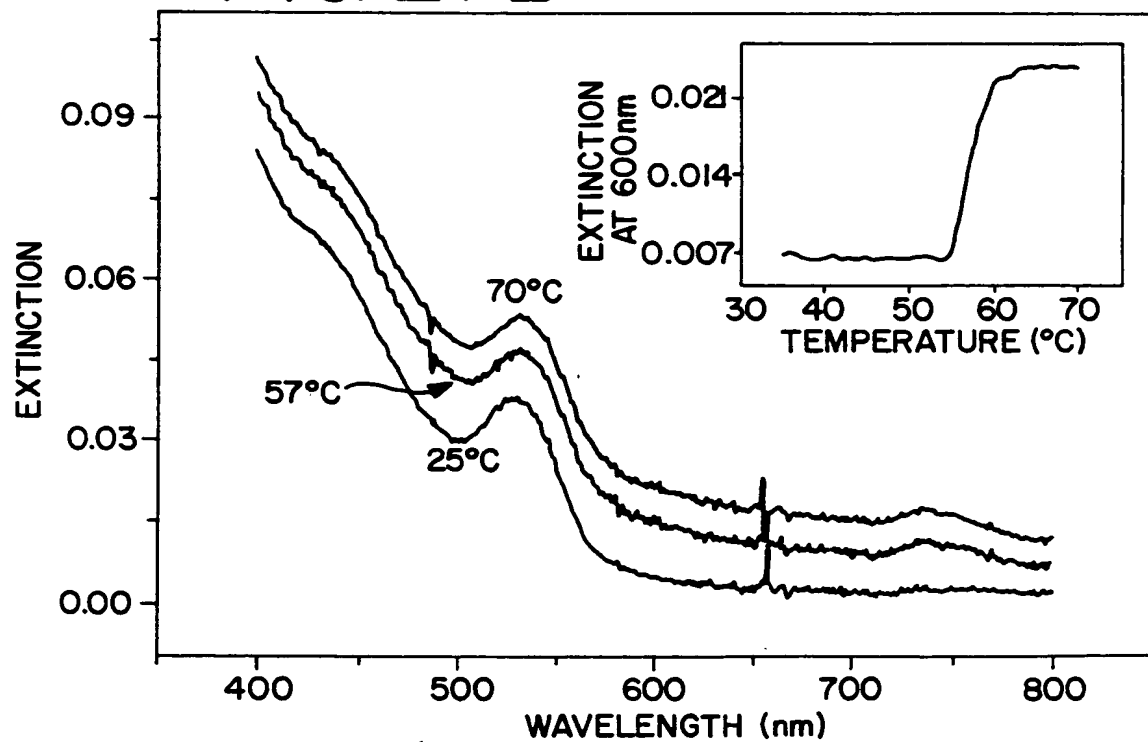


FIG. 27C

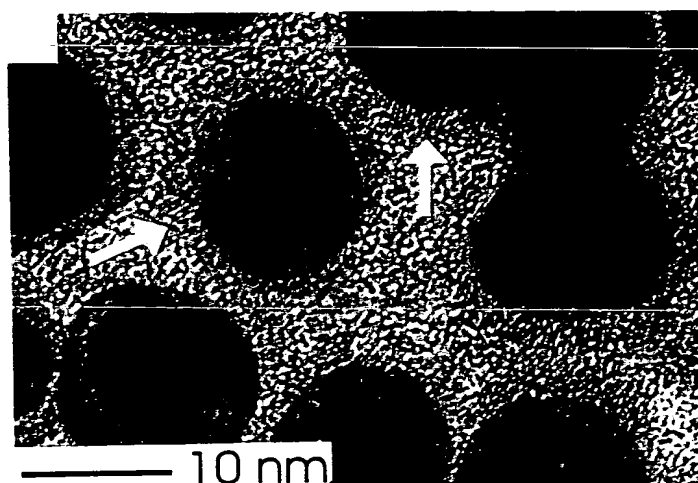


FIG. 27D

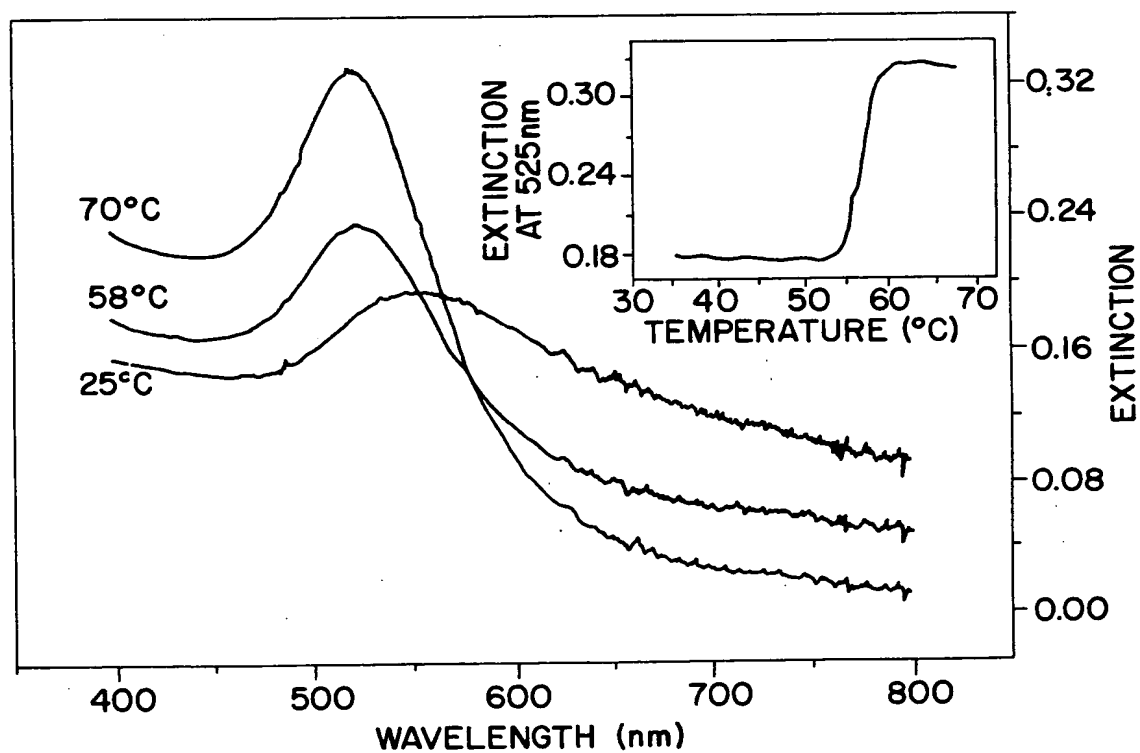
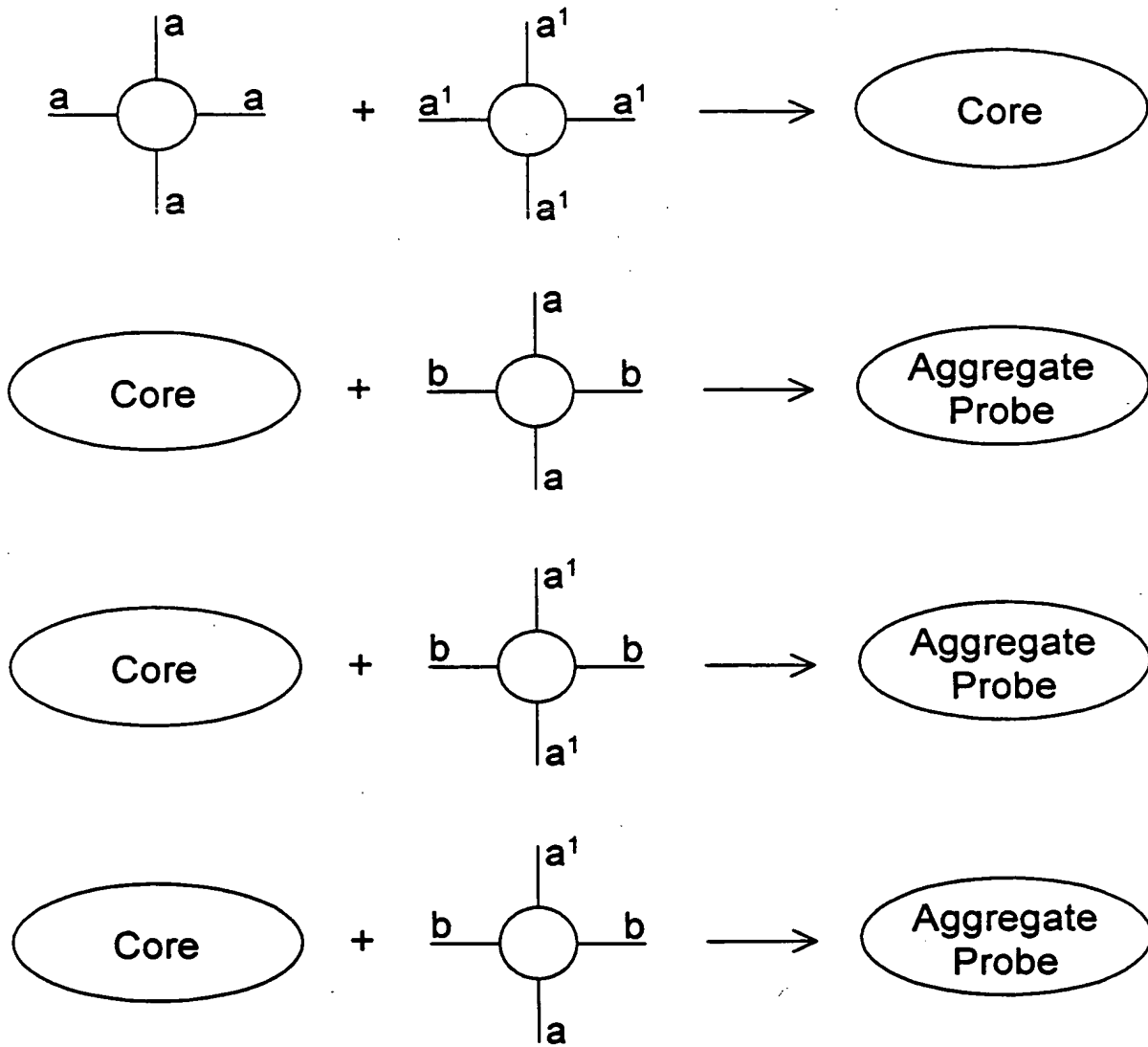


FIG. 28A



"Core" and "Aggregate Probe"

FIG. 28B

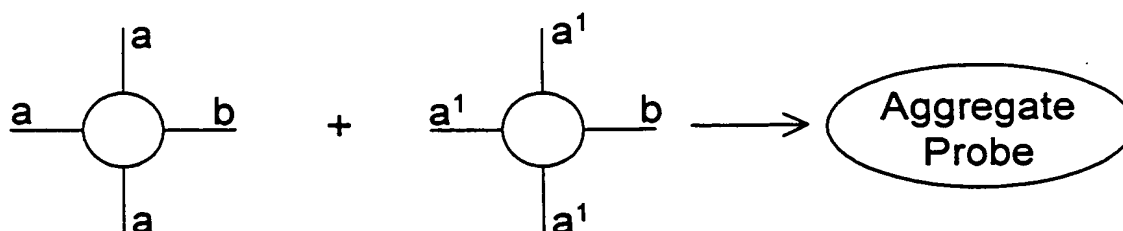


FIG. 28C

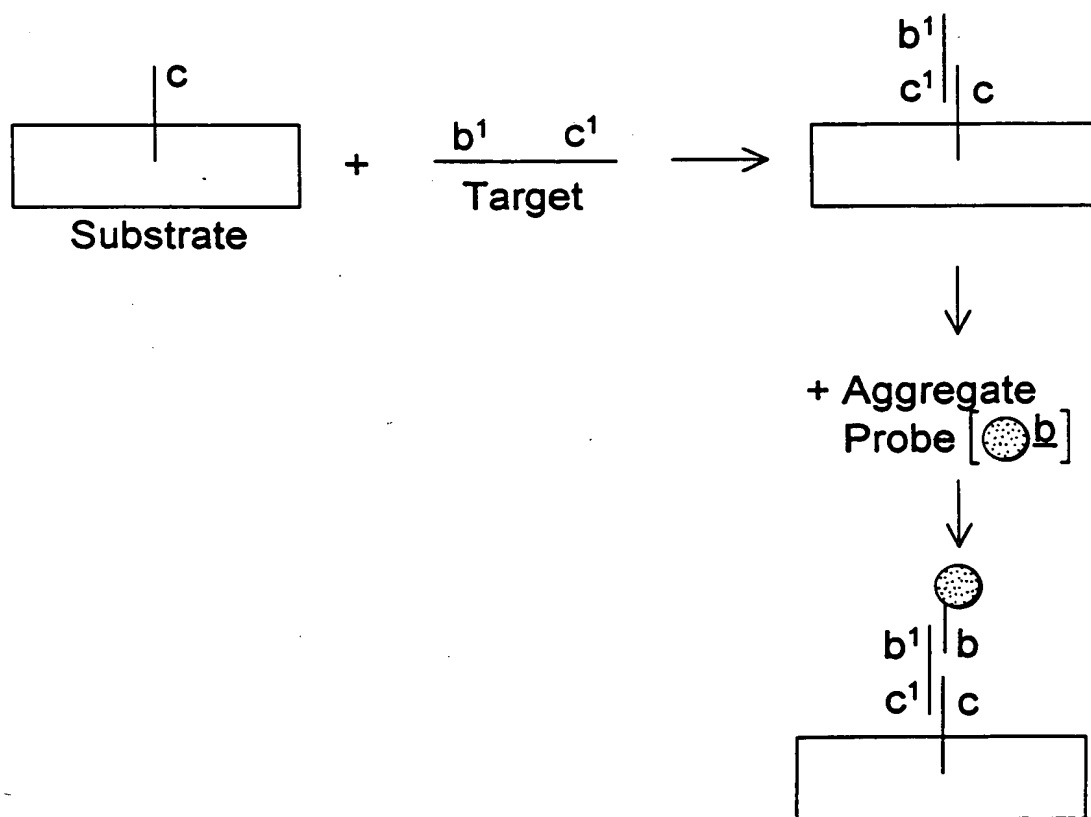


FIG. 28D

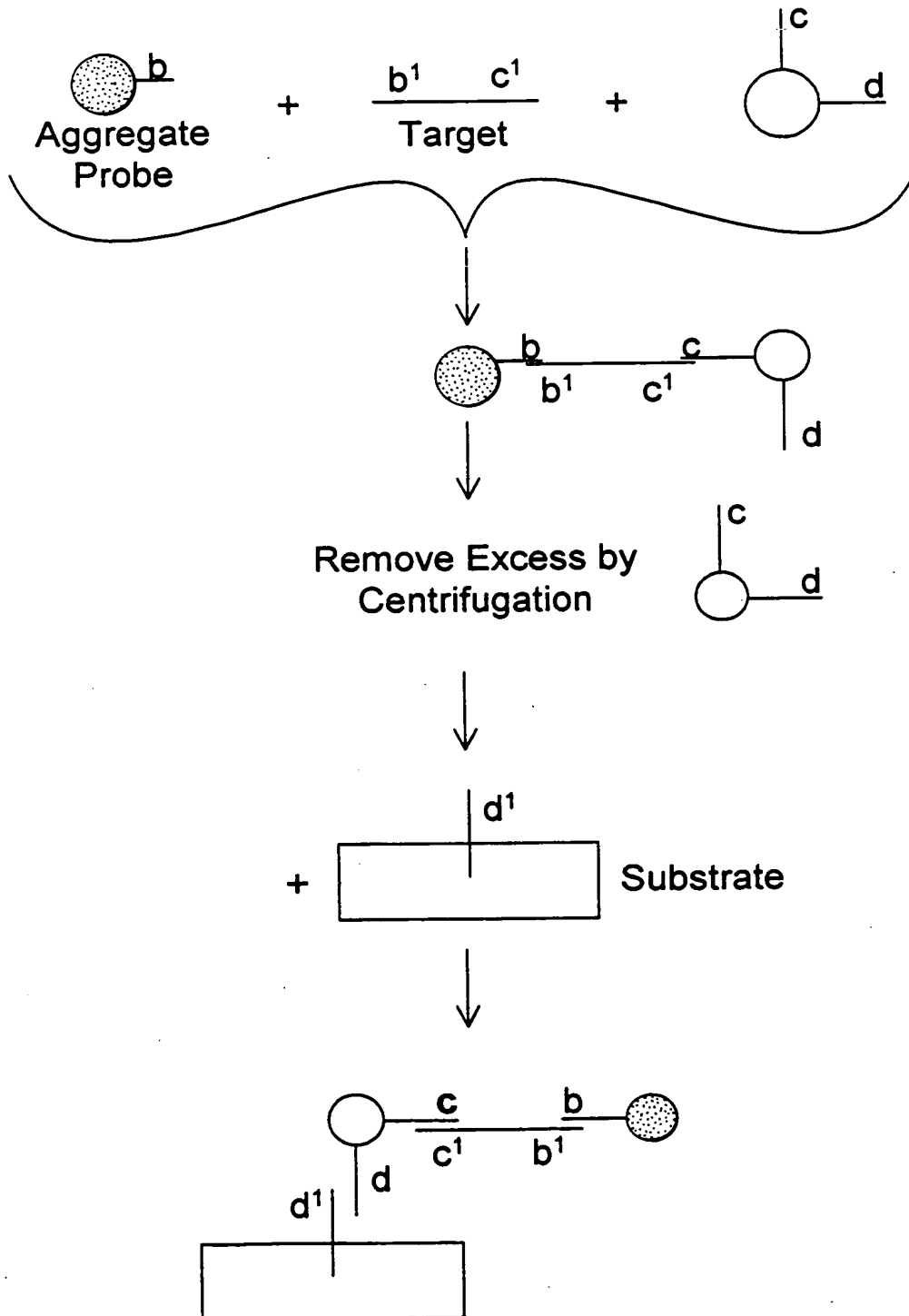
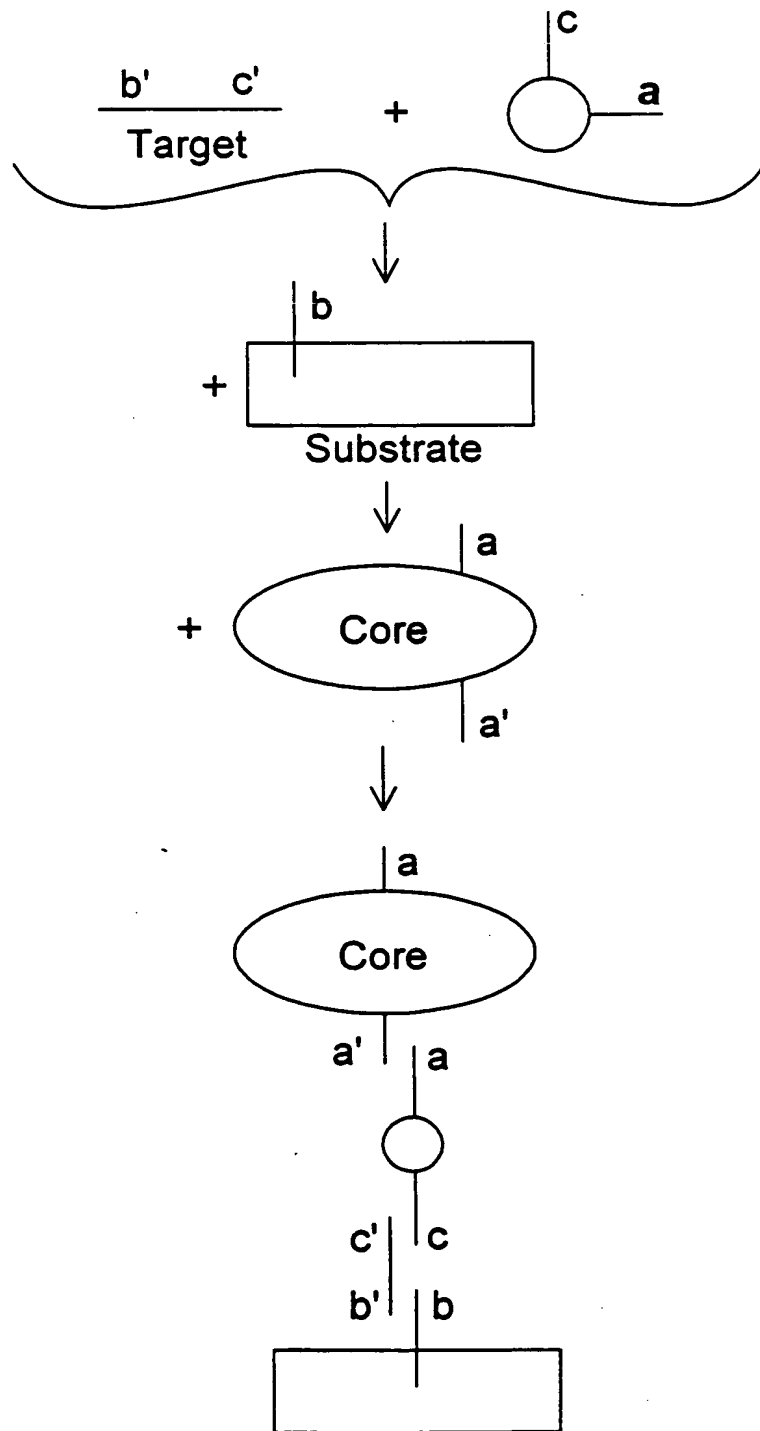
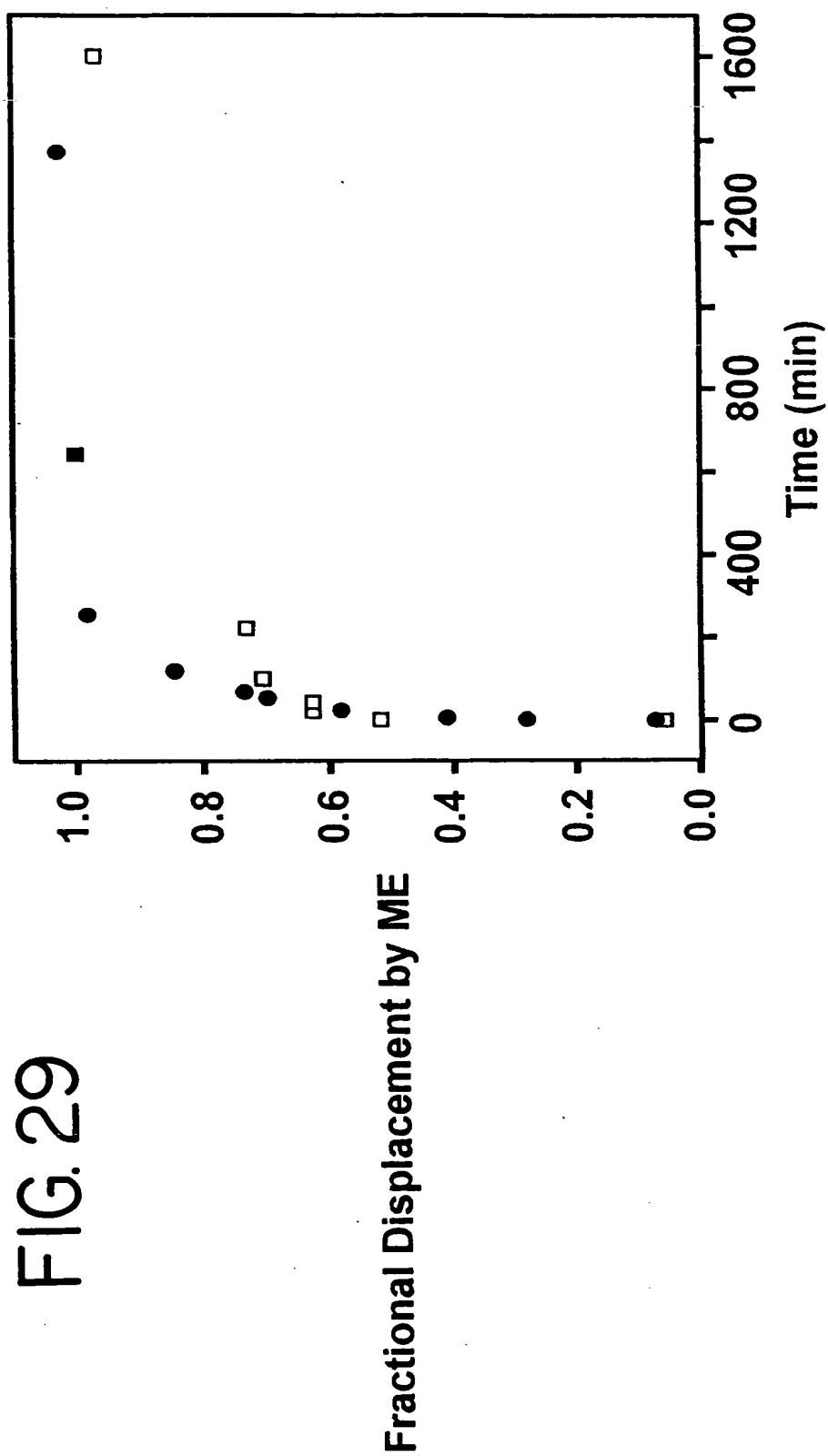
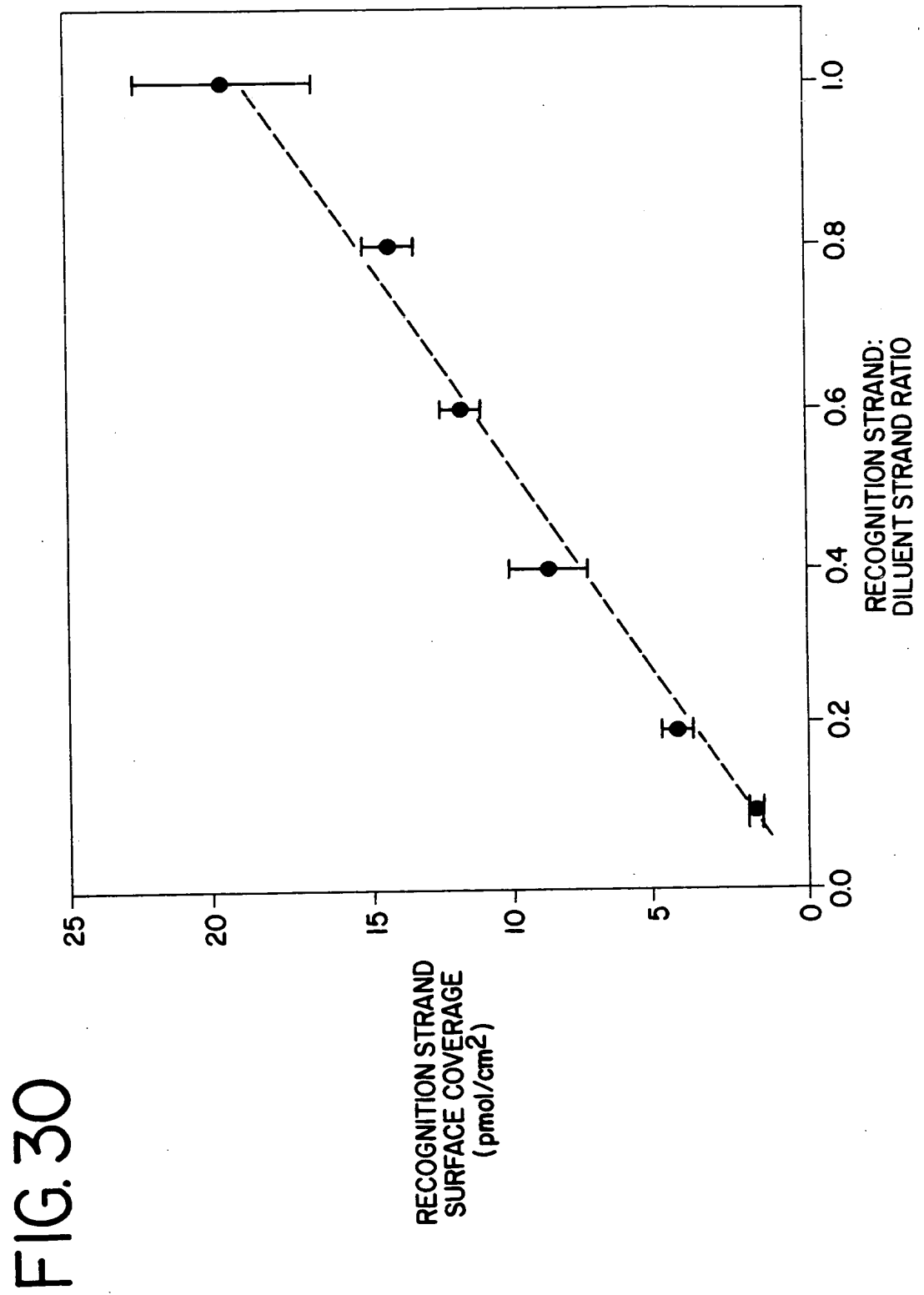


FIG. 28E







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FIG. 31

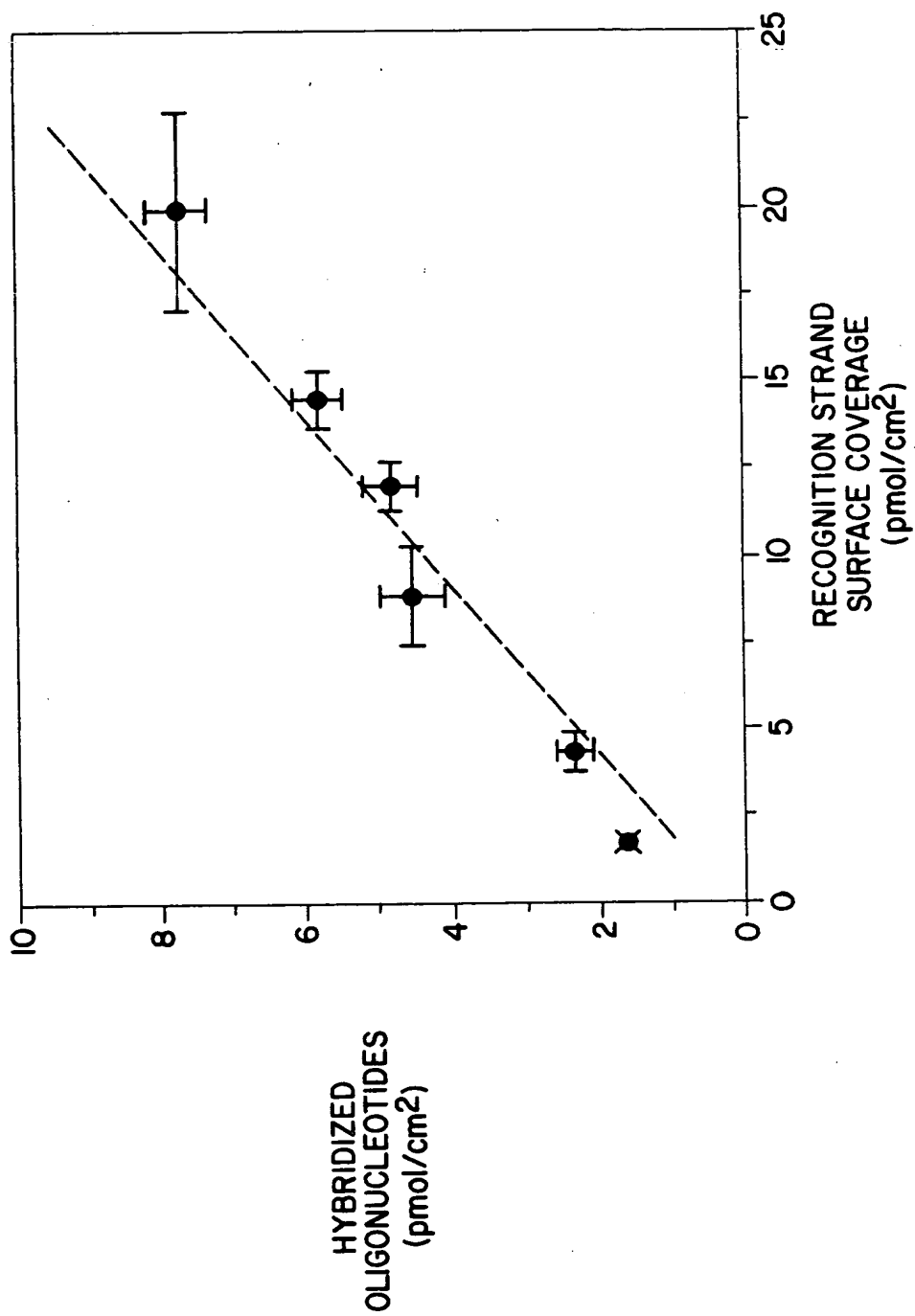
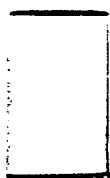


FIG. 33



A



B



C



D



E



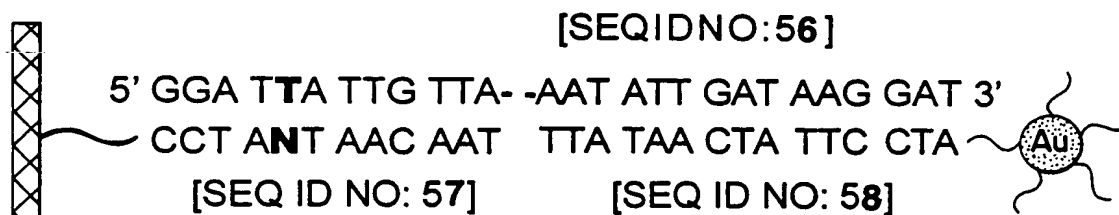
F



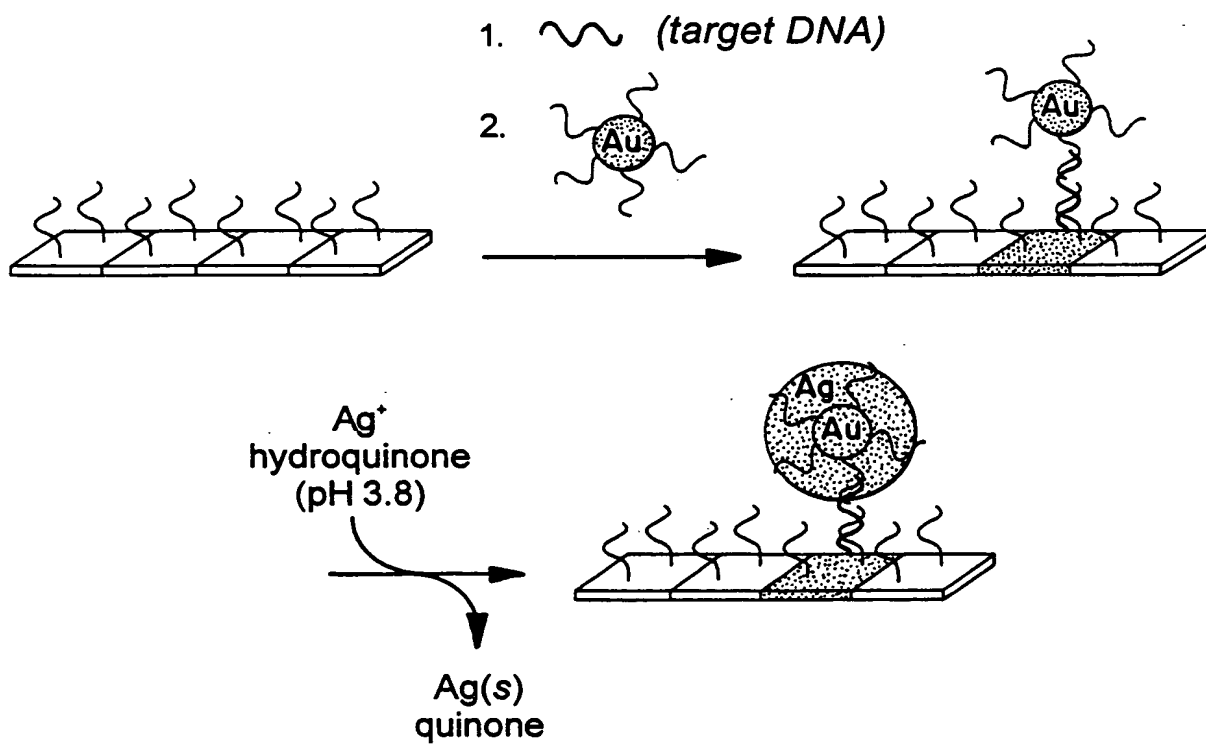
G

FIG. 33

FIG. 32



N = A (complementary),
G, C, T (mismatched)



T00T00" 2223555

FIG. 34

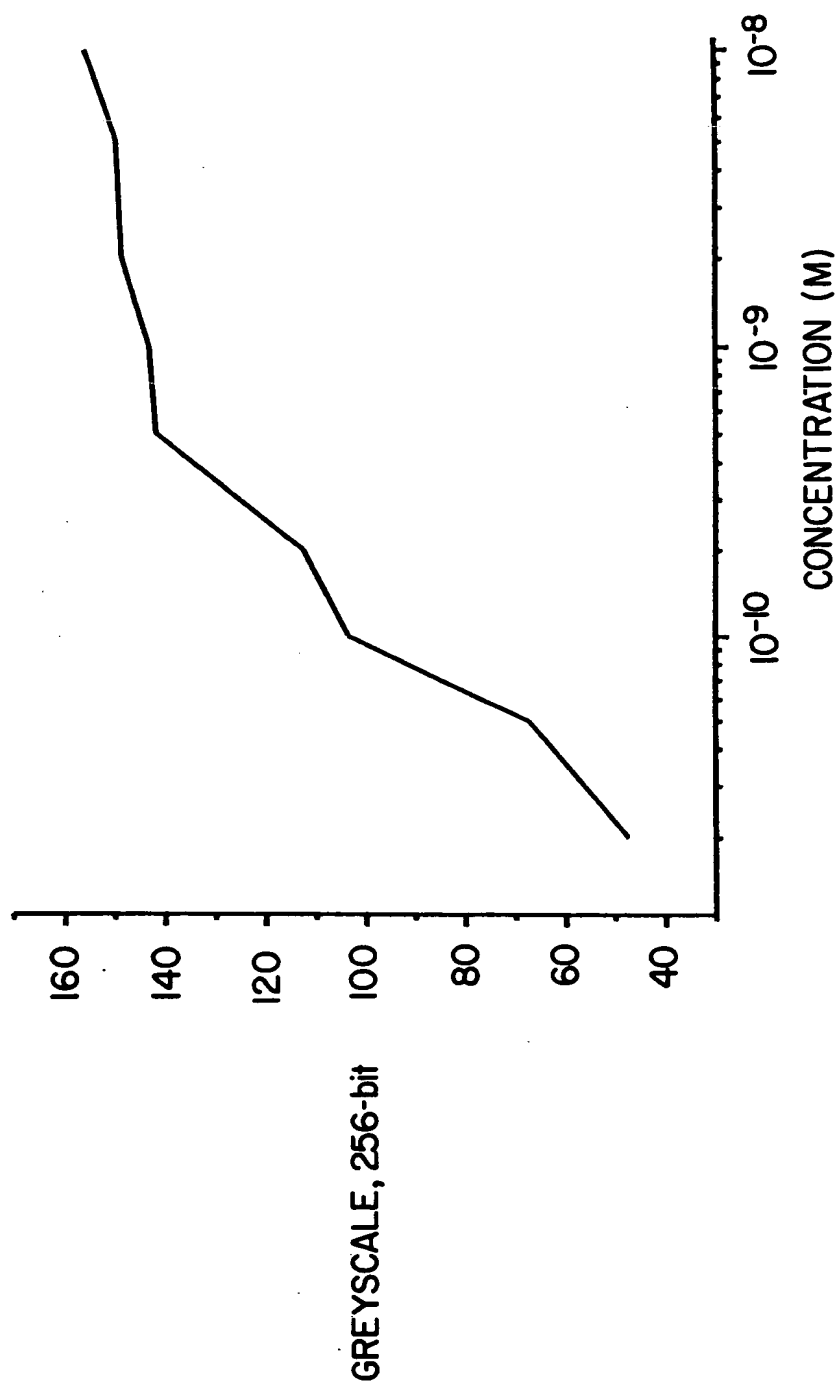


FIG.35A

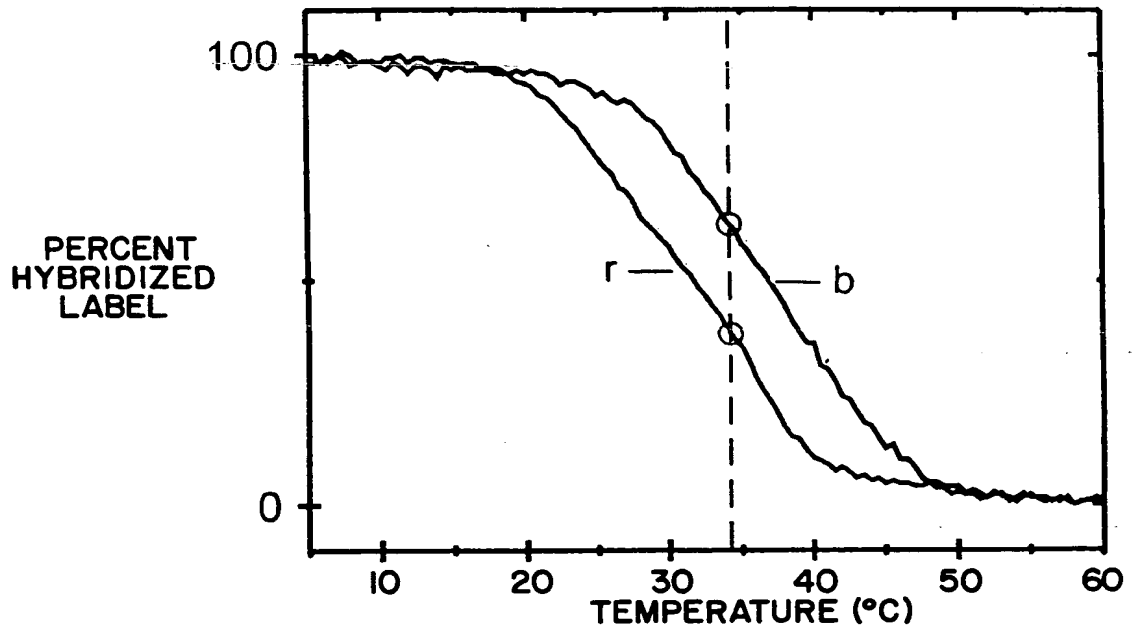


FIG.35B

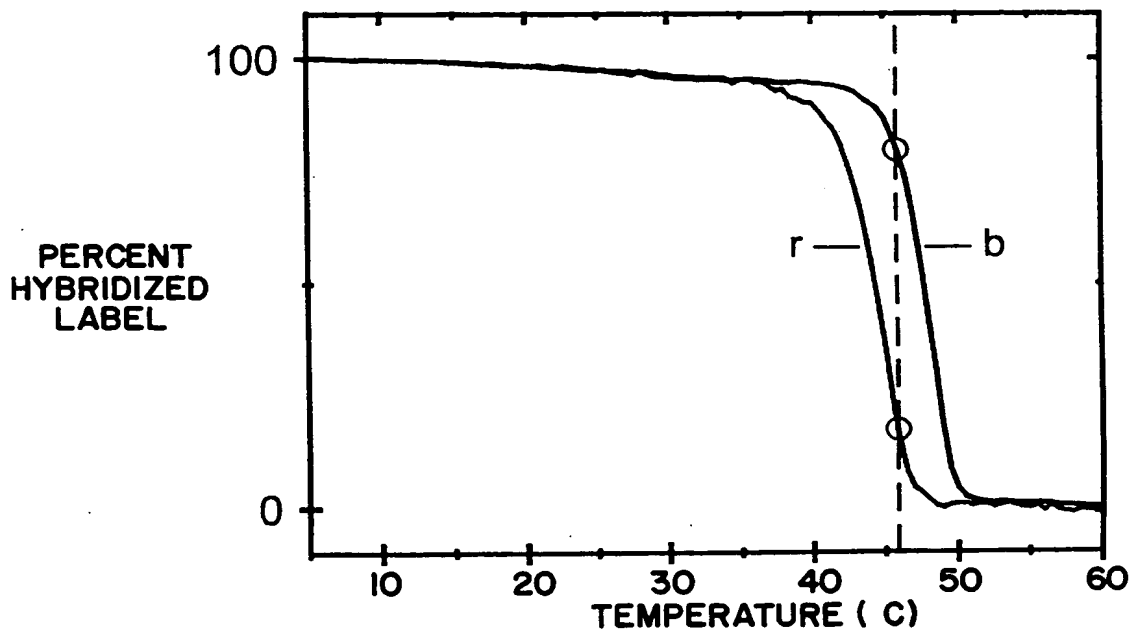


FIG. 36A

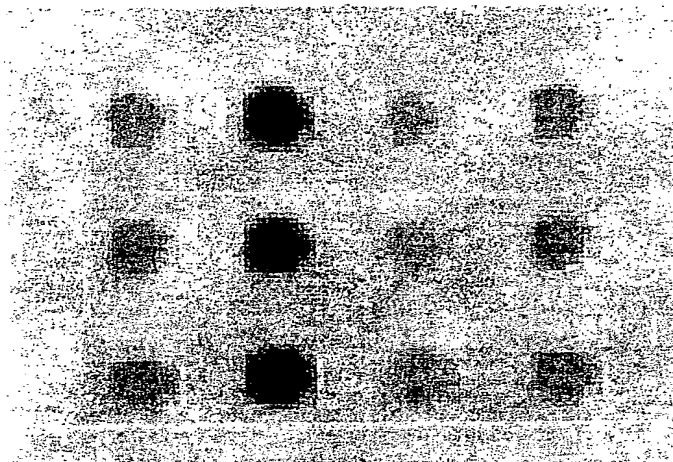
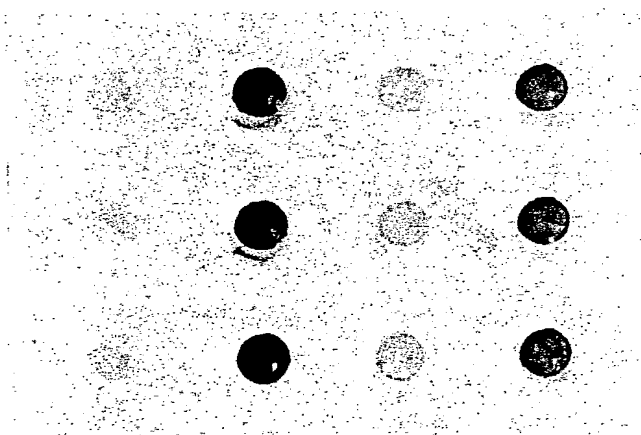


FIG. 36B



C A T G

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FIG.37A

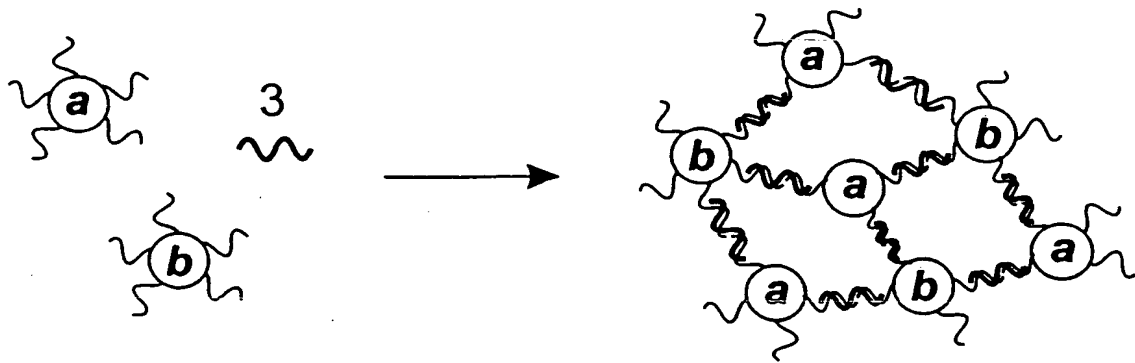


FIG.37B

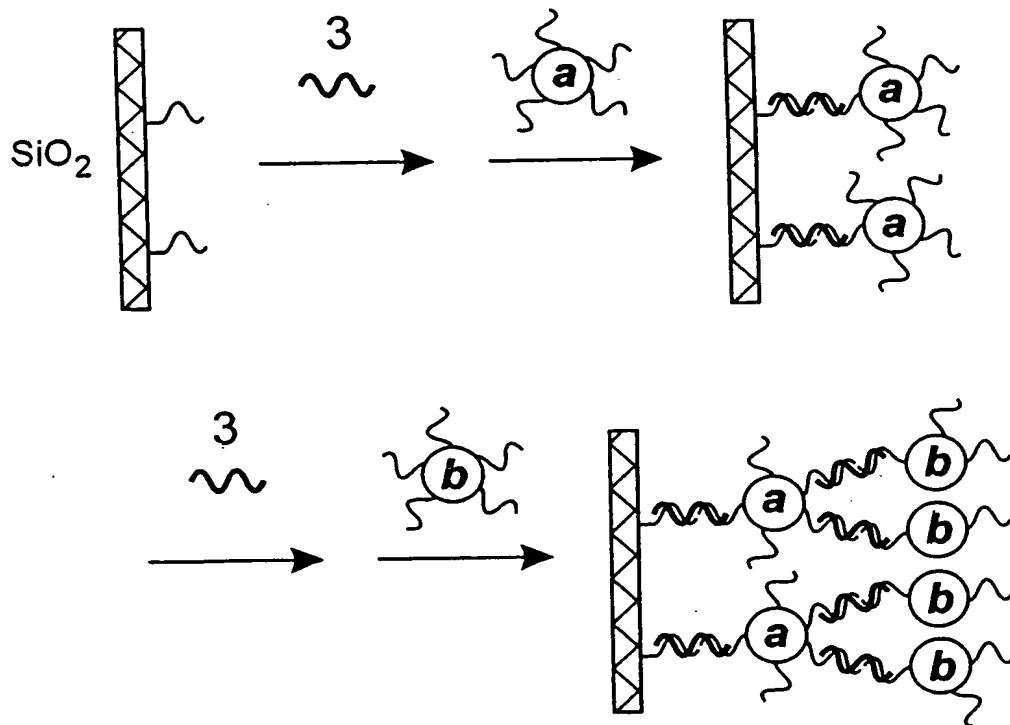


FIG.38A

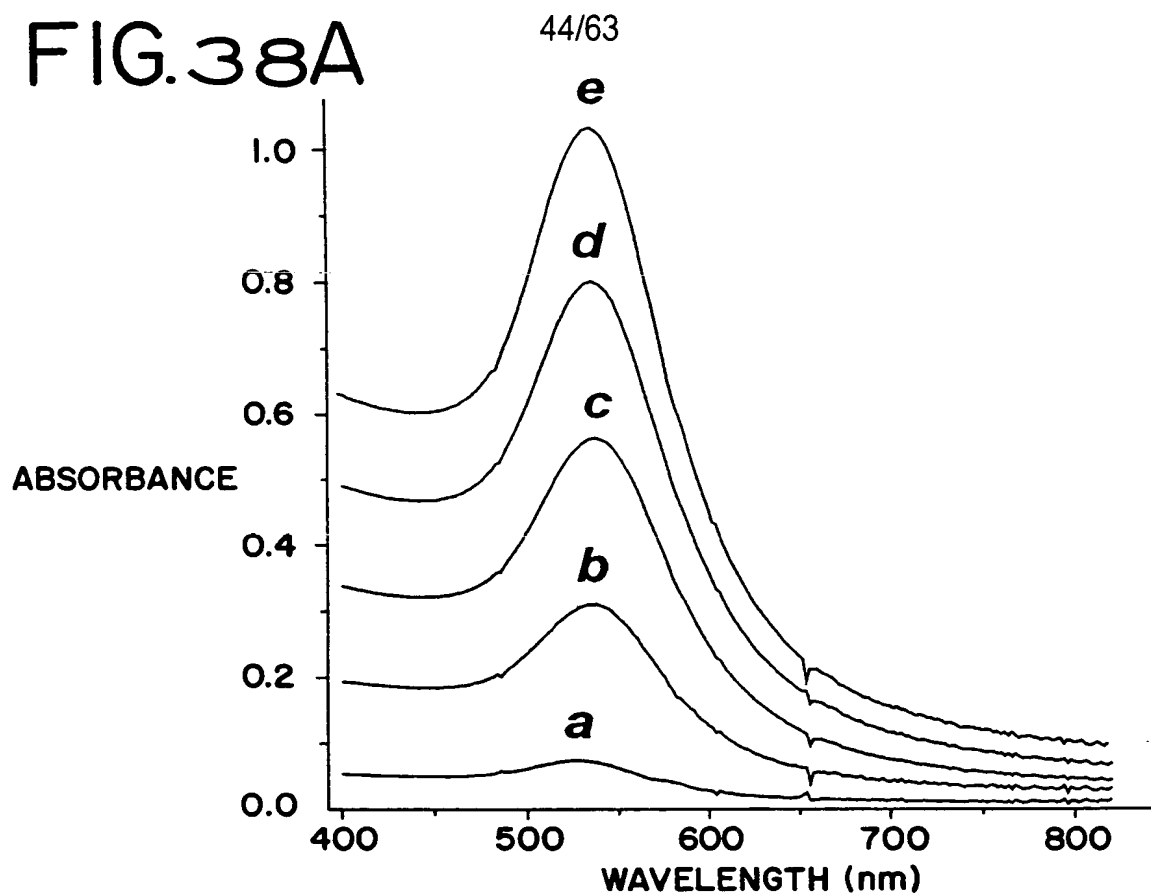


FIG.38B

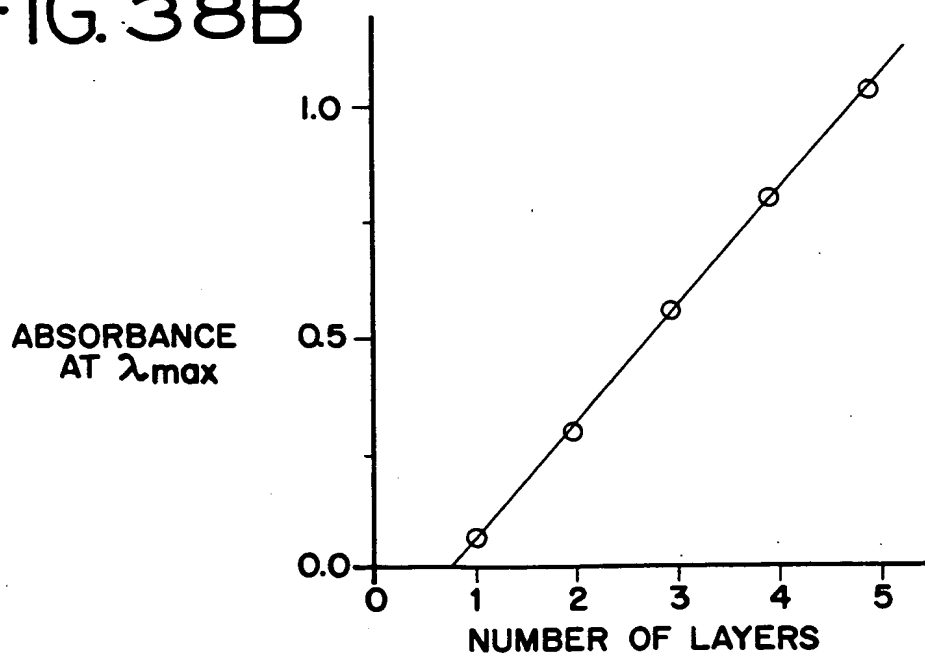


FIG. 39A

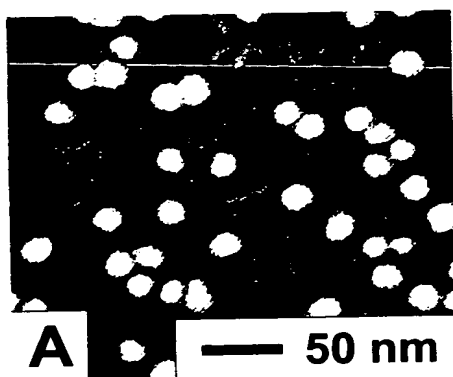
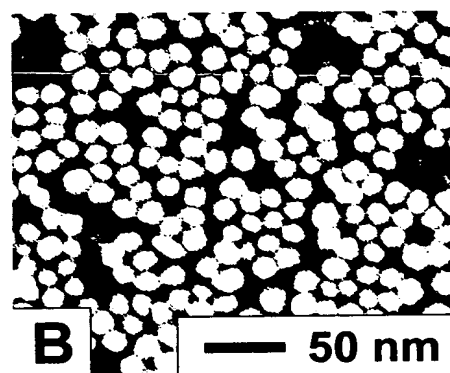


FIG. 39B



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FIG.39C

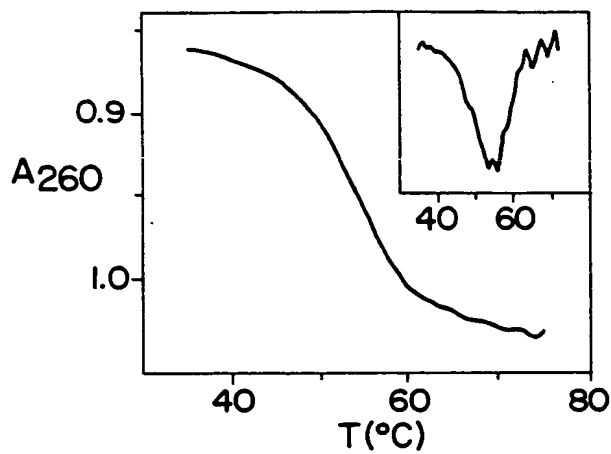


FIG.39D

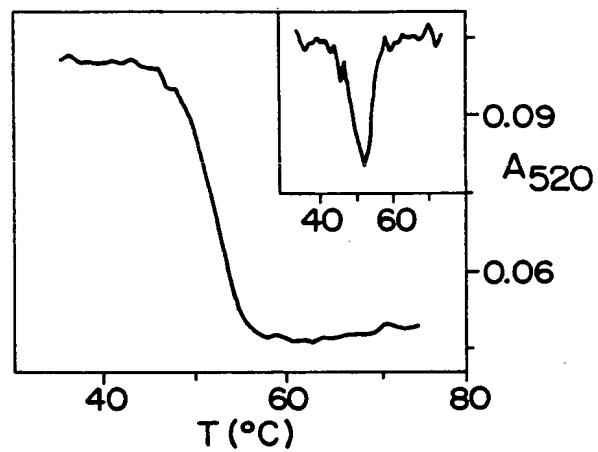


FIG.39E

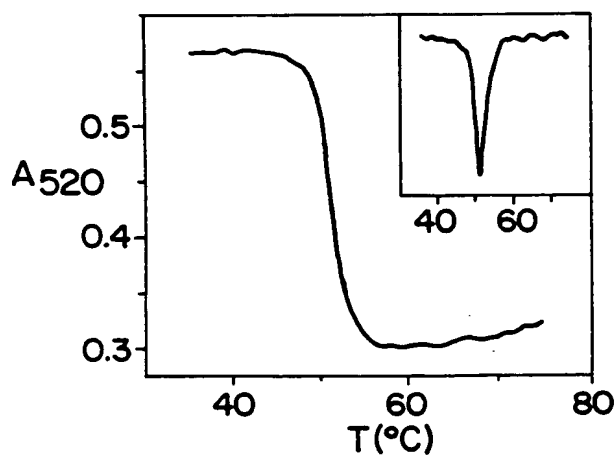
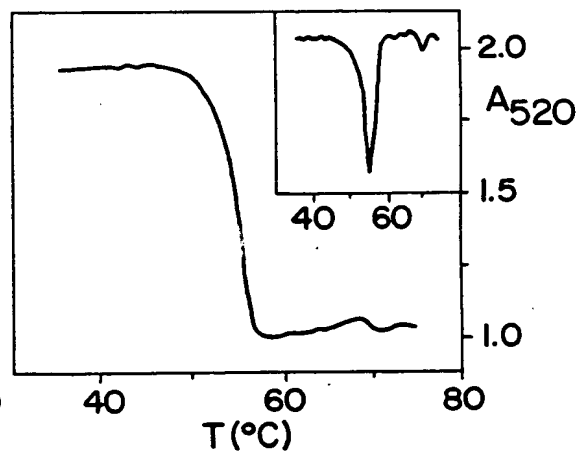


FIG.39F



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FIG. 40

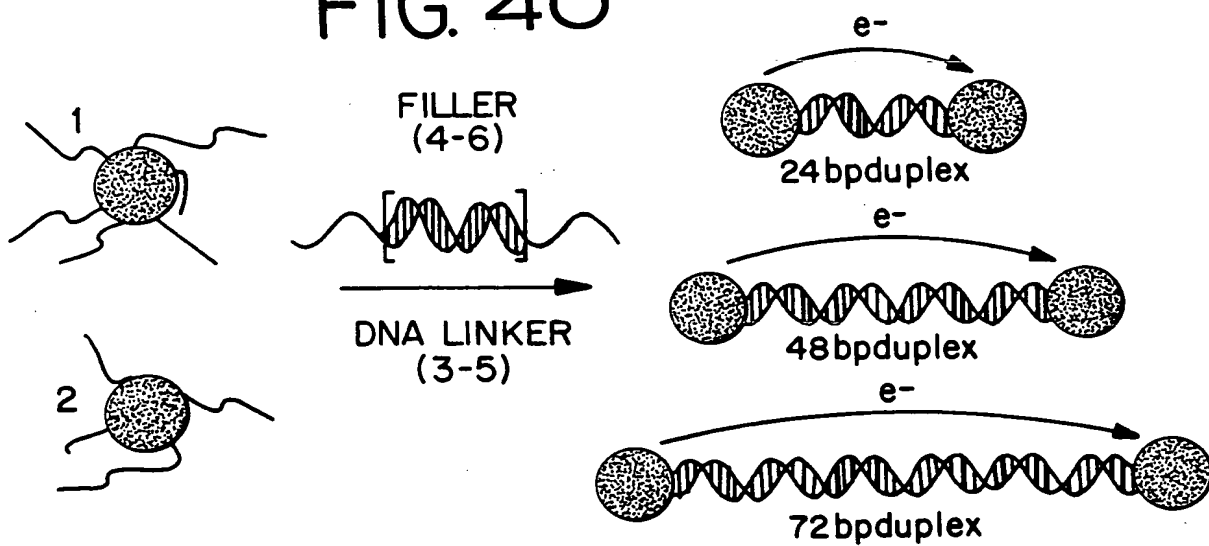


FIG. 41

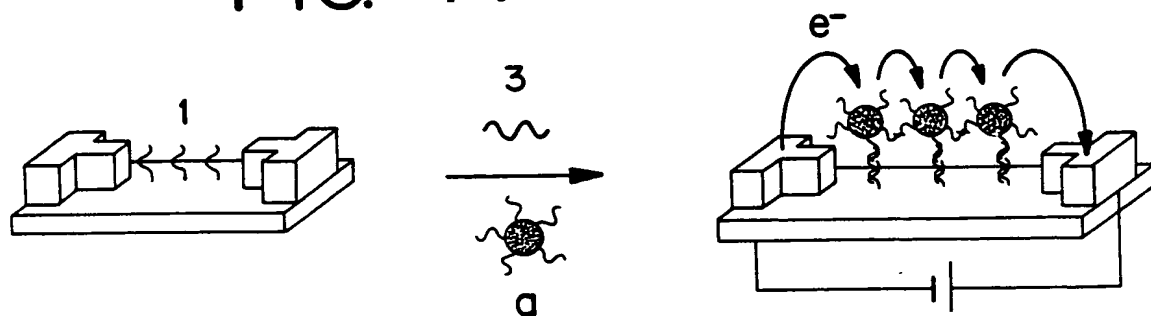
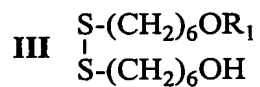
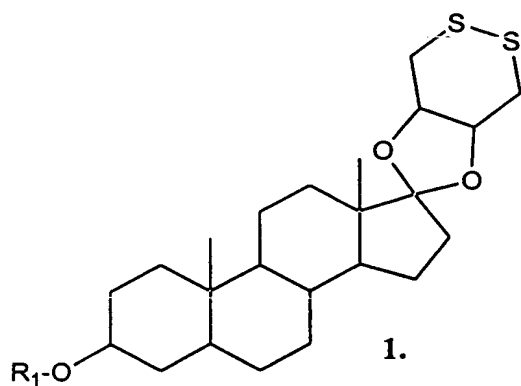


FIG. 42



R₁

a = H

b = (iPr)₂NP(OCH₂CH₂CN)-

c1 = 5'-p(A₂₀)-TATCGTTCCATCAGCT [SEQ ID NO: 65]

c2 = 5'-p(A₂₀)-TTGATCTTCCGTTCT [SEQ ID NO: 66]

Target I = 79-mer oligonucleotide with target region:

3'-.....ATAGCAAGGTAGTCGAGCAACTAGAAAGGCAAGA.....5'
[SEQ ID NO: 67]

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9

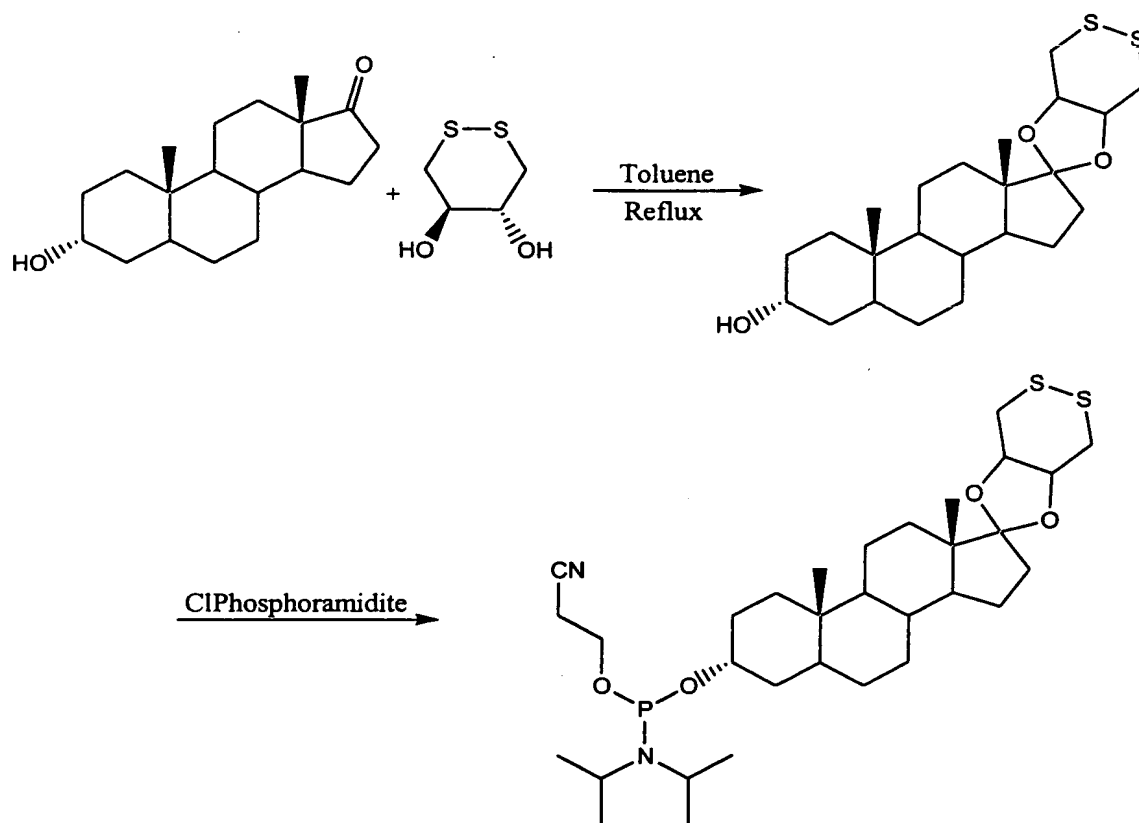
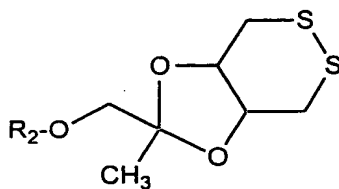


FIG. 44



2.

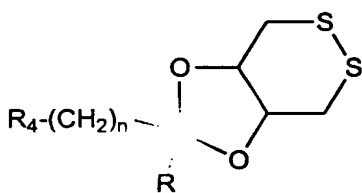
 R_2

a = H

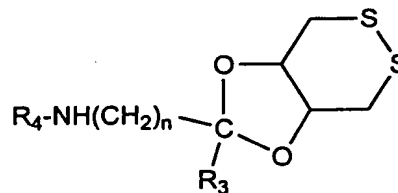
b = (iPr)₂NP(OCH₂CH₂CN)-c1 = 5'-p(A₂₀)-GCAGACCTCA [SEQ ID NO: 68]c2 = 5'-p(A₂₀)-CCTATGTGTCG [SEQ ID NO: 69]D = 5'-p(A₂₀) [SEQ ID NO: 70]

Target I = 63-mer oligonucleotide with target region:

3'-.....CGTCTGGAGTGGATACACAGC.....5'
[SEQ ID NO: 71]



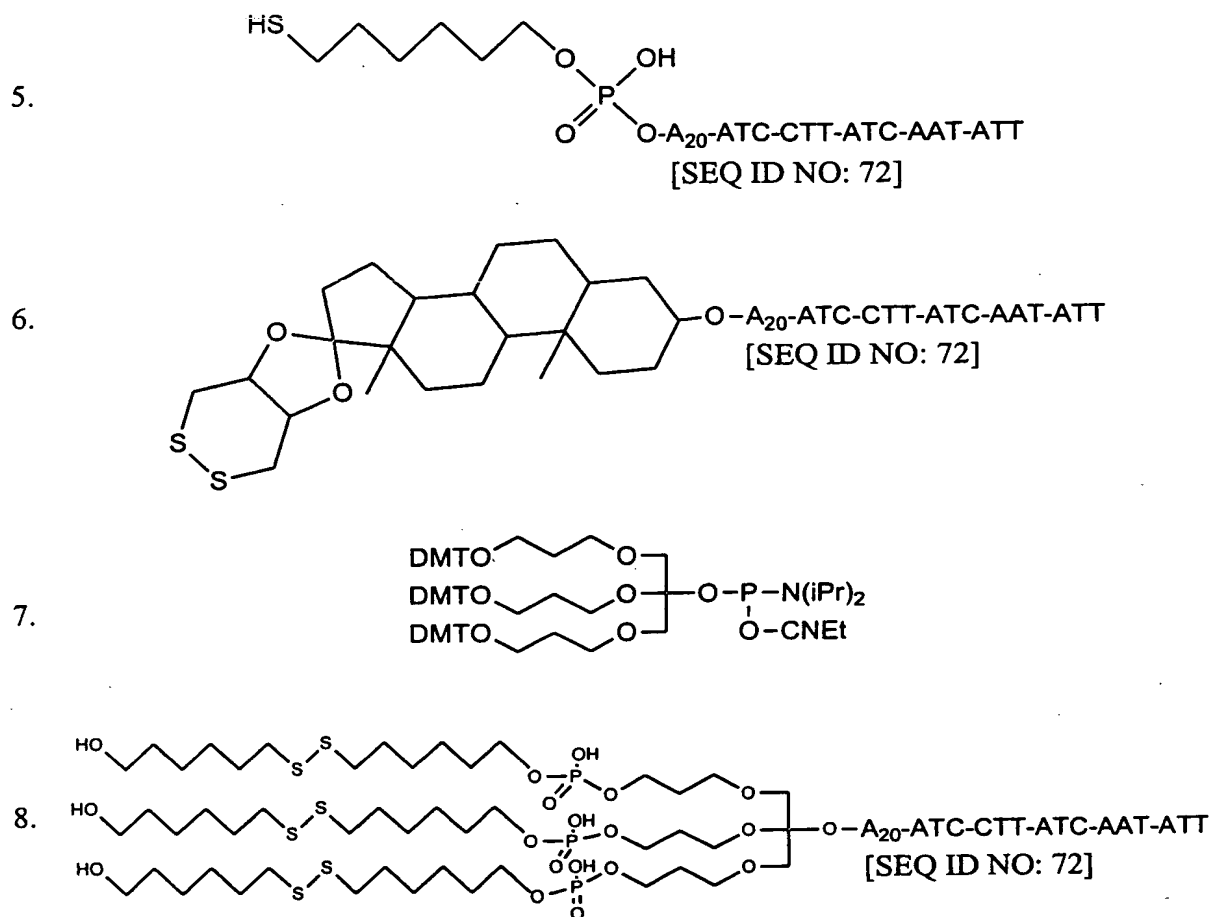
3.



4.

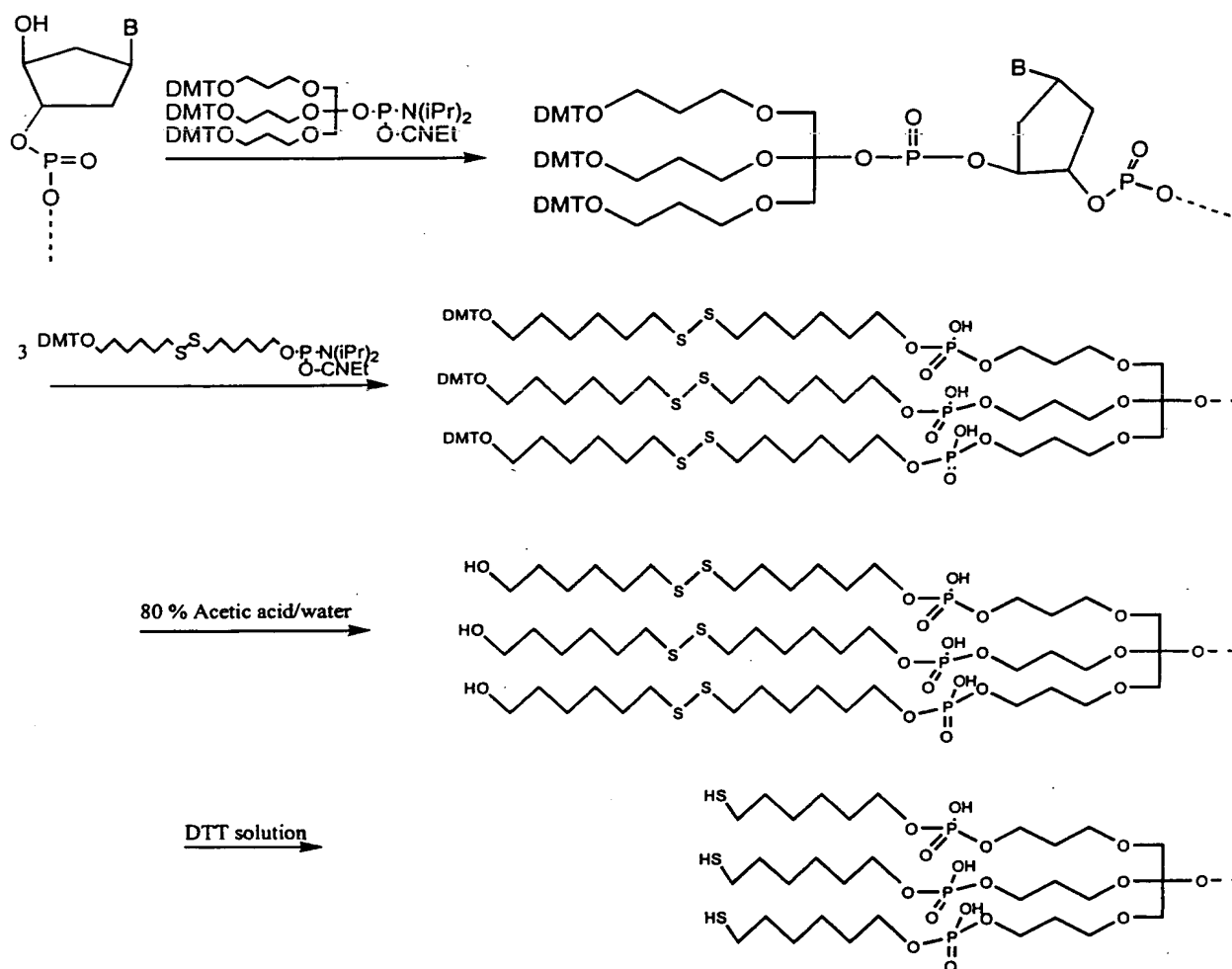
 R_3 = hydrogen, an alkyl group, an aryl group, or a substituted alkyl or aryl group R_4 = an attached oligonucleotide or modified oligonucleotide

FIG. 45



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FIG. 46



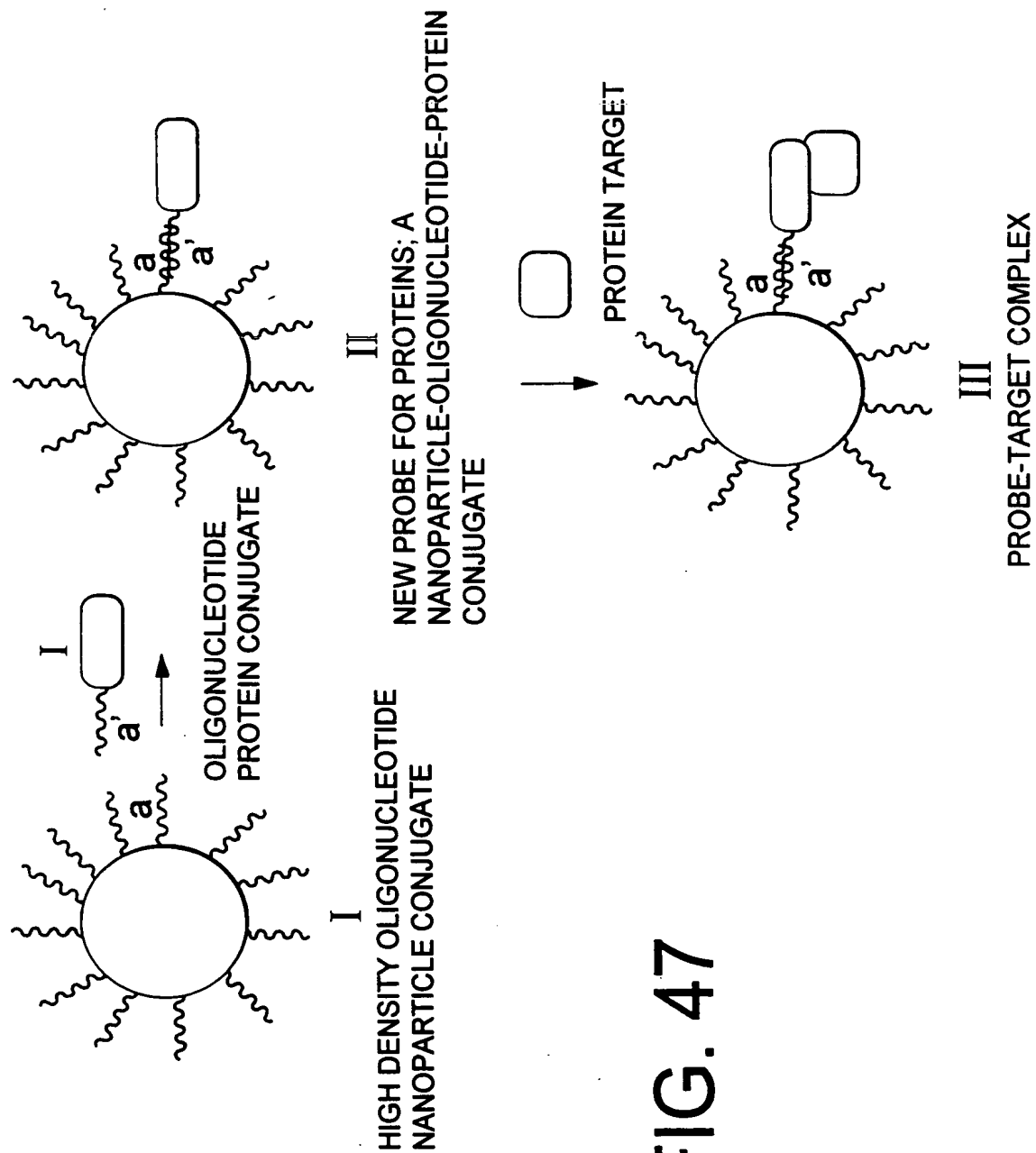
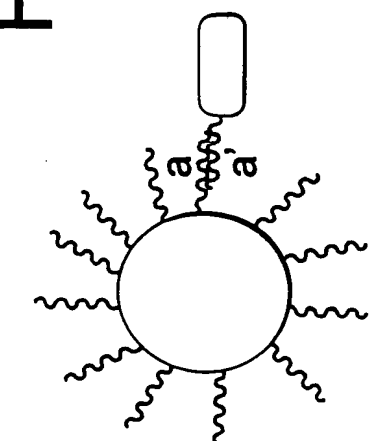


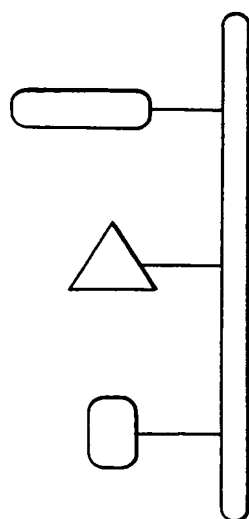
FIG. 47

FIG. 48



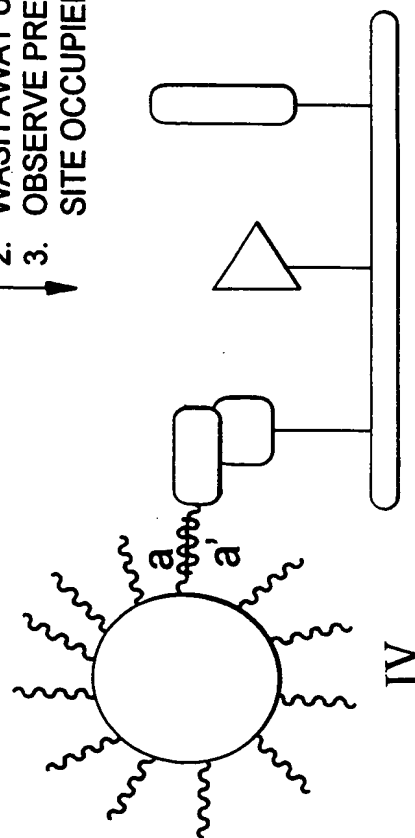
II

NEW PROBE FOR PROTEINS; A
NANOPARTICLE-OLIGONUCLEOTIDE-PROTEIN
CONJUGATE

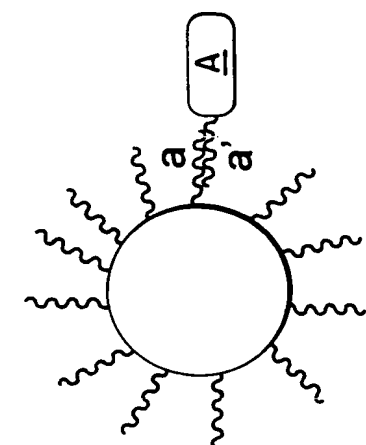


GLASS PLATE WITH THREE DIFFERENT PROTEINS
IMMOBILIZED ON THE SURFACE, ONE OF WHICH
BINDS TO THE PROTEIN IN PROBE II

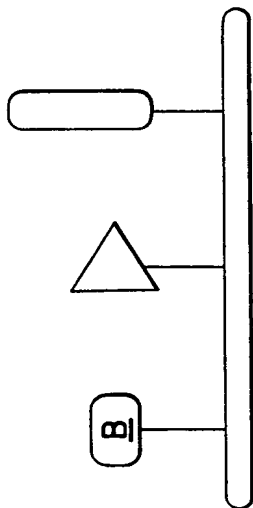
1. EXPOSE PLATE TO THE PROBE SOLUTION
2. WASH AWAY UNBOUND NANOPARTICLE PROBE
3. OBSERVE PRESENCE OF BOUND NANOPARTICLES AT
SITE OCCUPIED BY THE FIRST PROTEIN IN THE SERIES.



IV



II'
NANOPARTICLE-OLIGONUCLEOTIDE-RECEPTOR



GLASS PLATE WITH THREE DIFFERENT SUBSTANCES
IMMOBILIZED ON THE SURFACE, ONE OF WHICH (B)
BINDS TO THE RECEPTOR UNIT (A) IN II'.

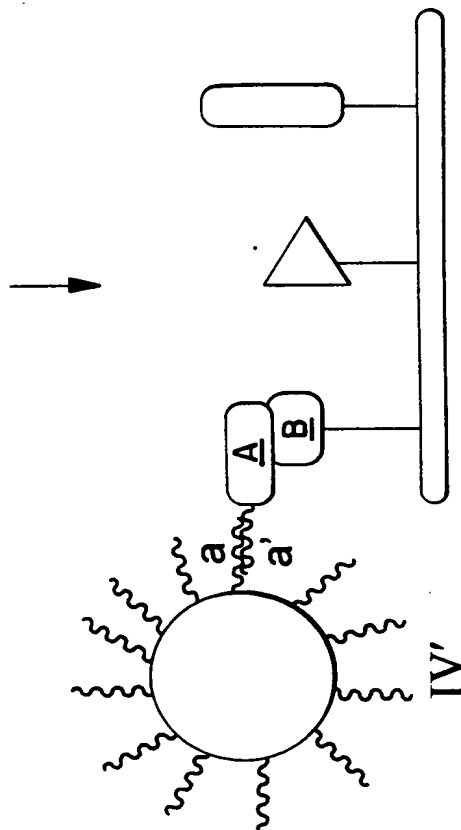


FIG. 49

FIG. 50A

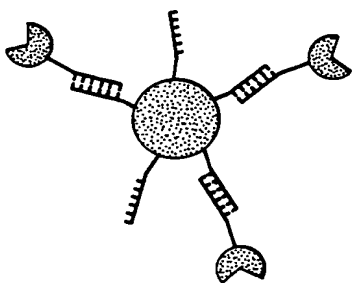


FIG. 50B

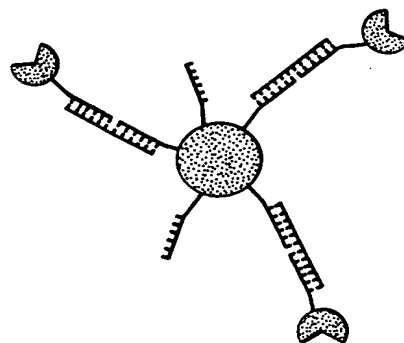


FIG. 51A

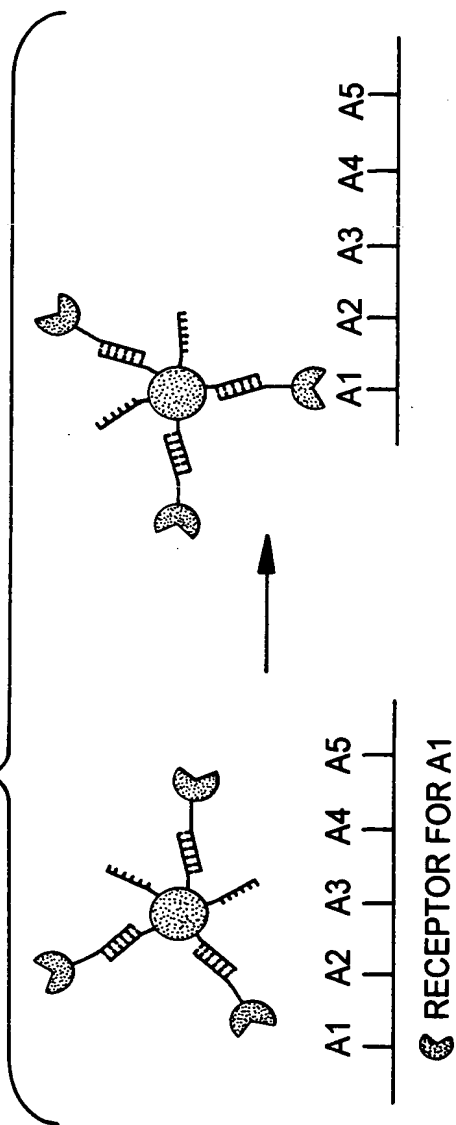


FIG. 51B

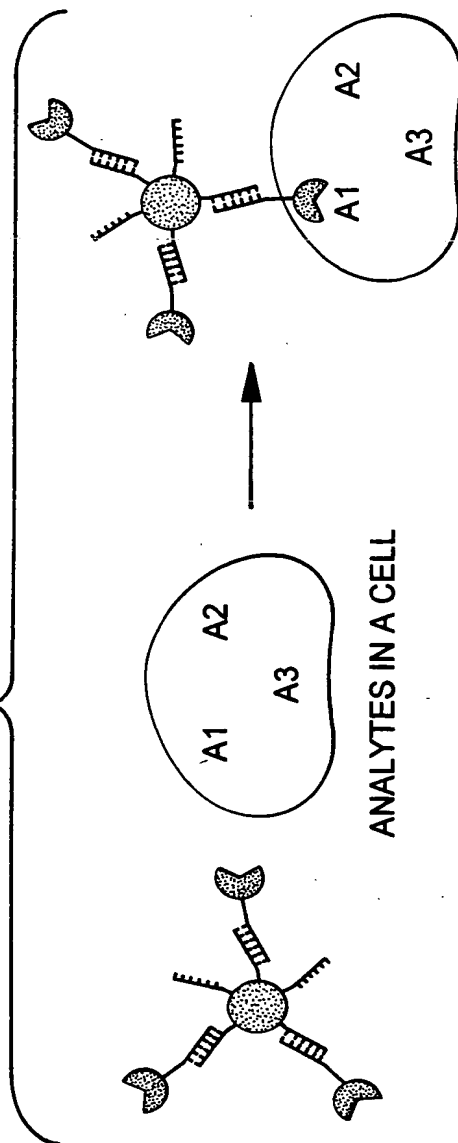
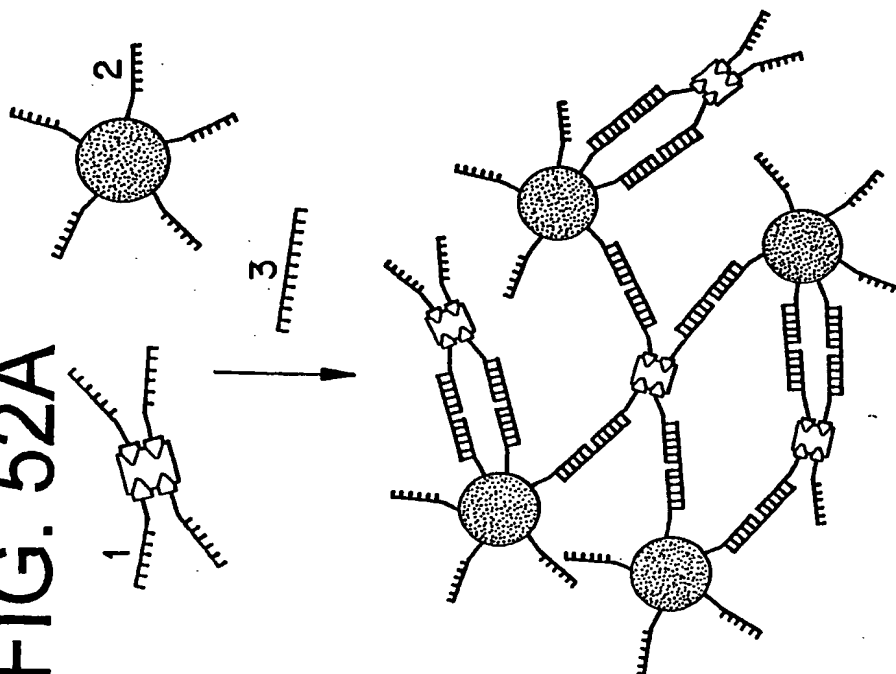


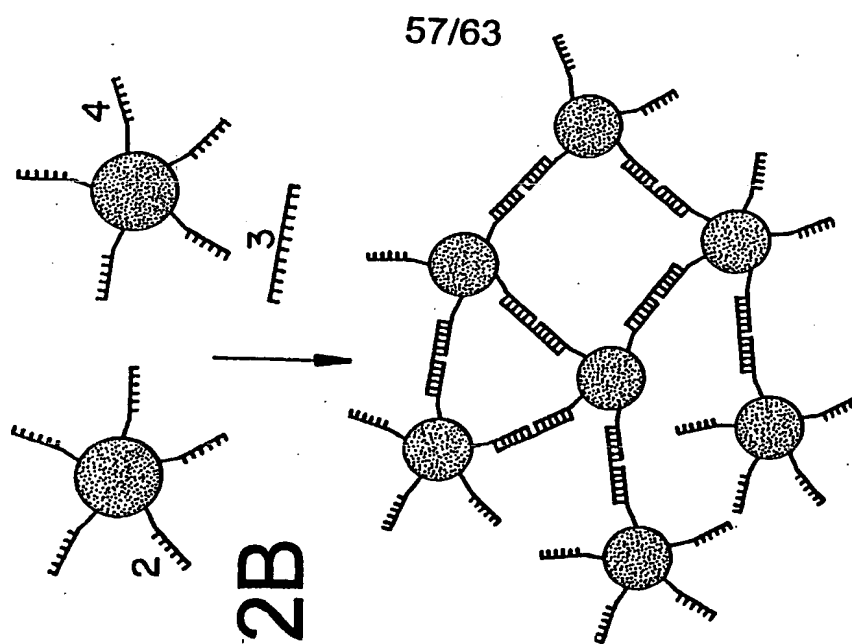
FIG. 52A



- 1 3' biotin-TEG-A₁₀-ATG CTC AAC TCT 5' [SEQ. ID NO. 73]
 2 5' SH(CH₂)₆-A₁₀-CGC ATT CAG GAT 3' [SEQ. ID NO. 74]
 3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3' [SEQ. ID NO. 75]

● 13 nm Au NANOPARTICLES [W] STREPTAVIDIN

FIG. 52B



- 2 5' SH(CH₂)₆-A₁₀-CGC ATT CAG GAT 3'
 3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3'
 4 3' SH(CH₂)₃-A₁₀-ATG CTC AAC TCT 5'

● 13 nm Au NANOPARTICLES

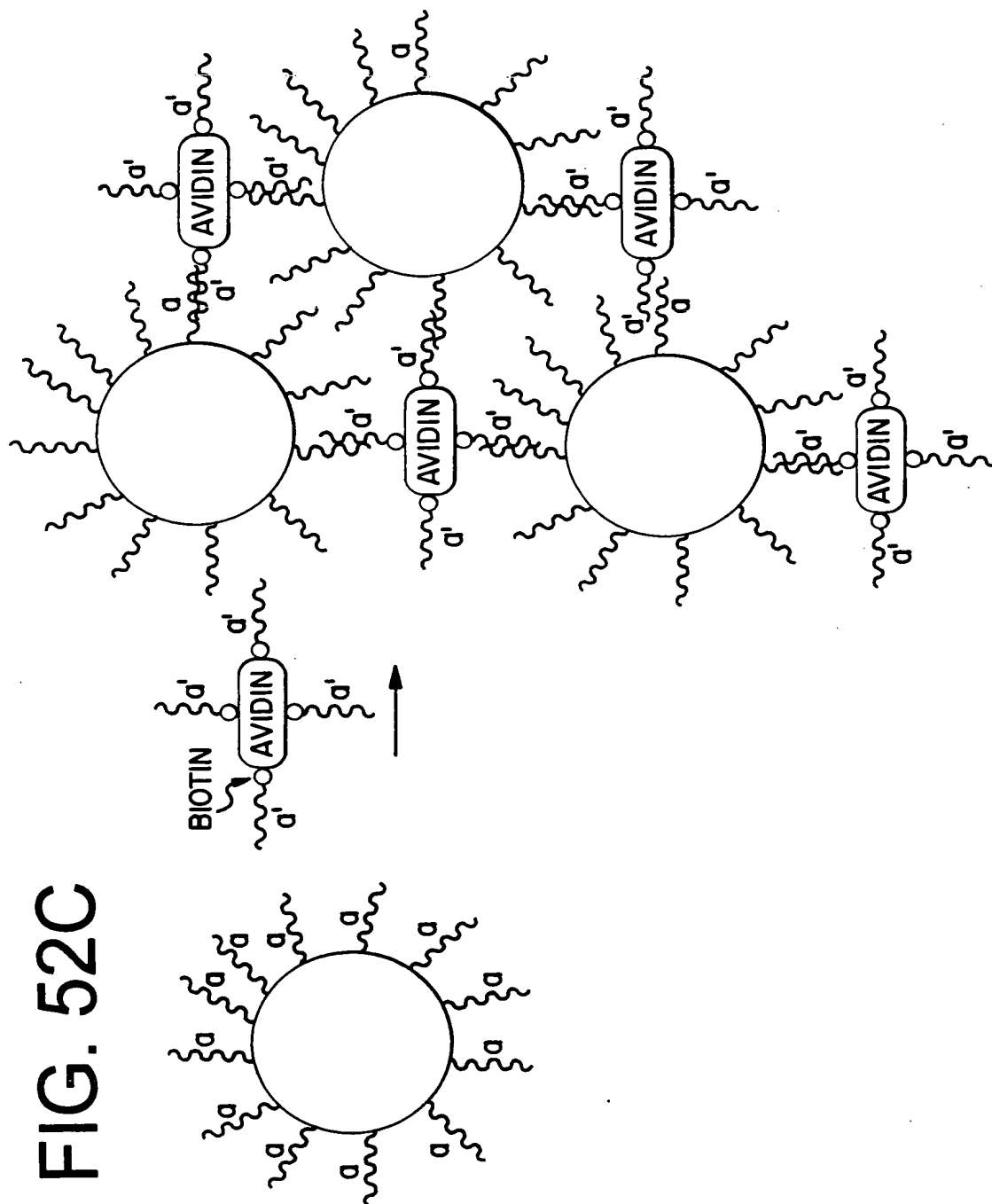


FIG. 55

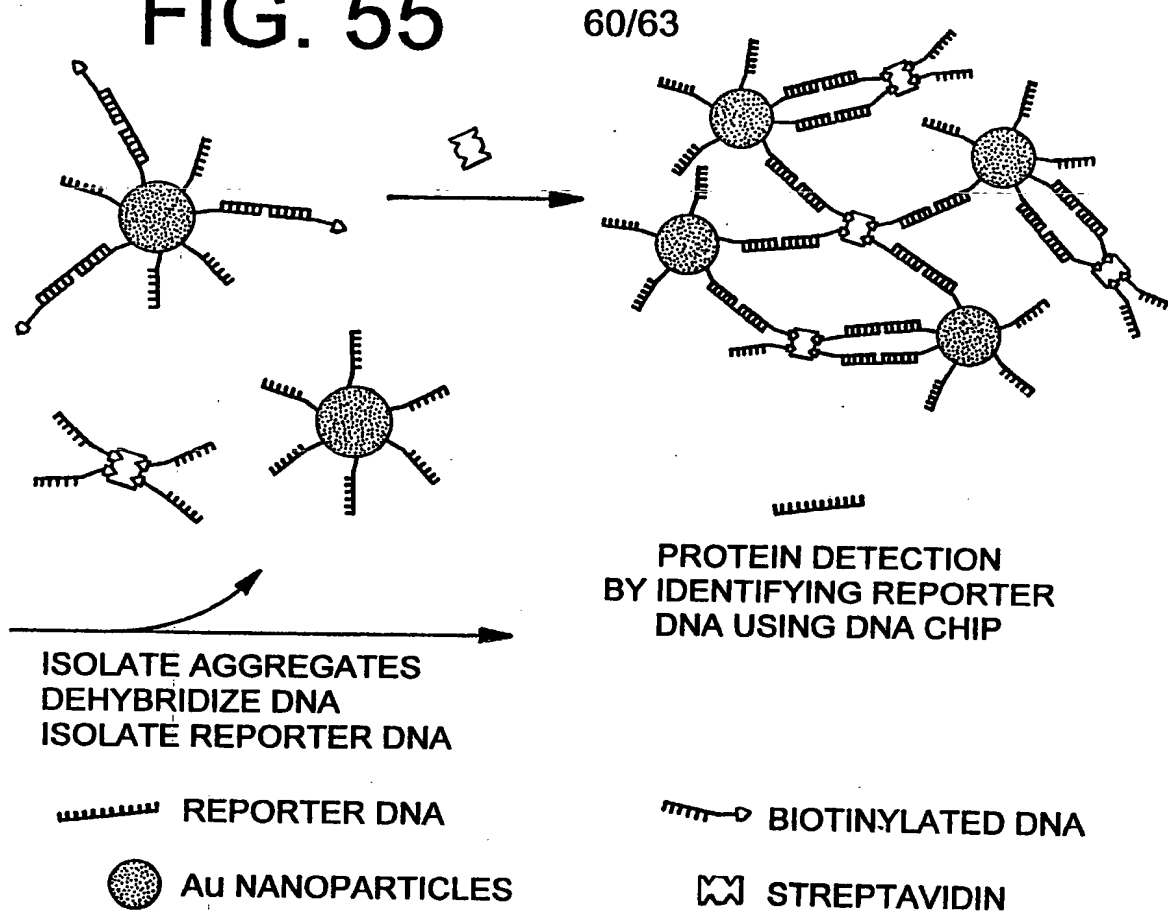


FIG. 56

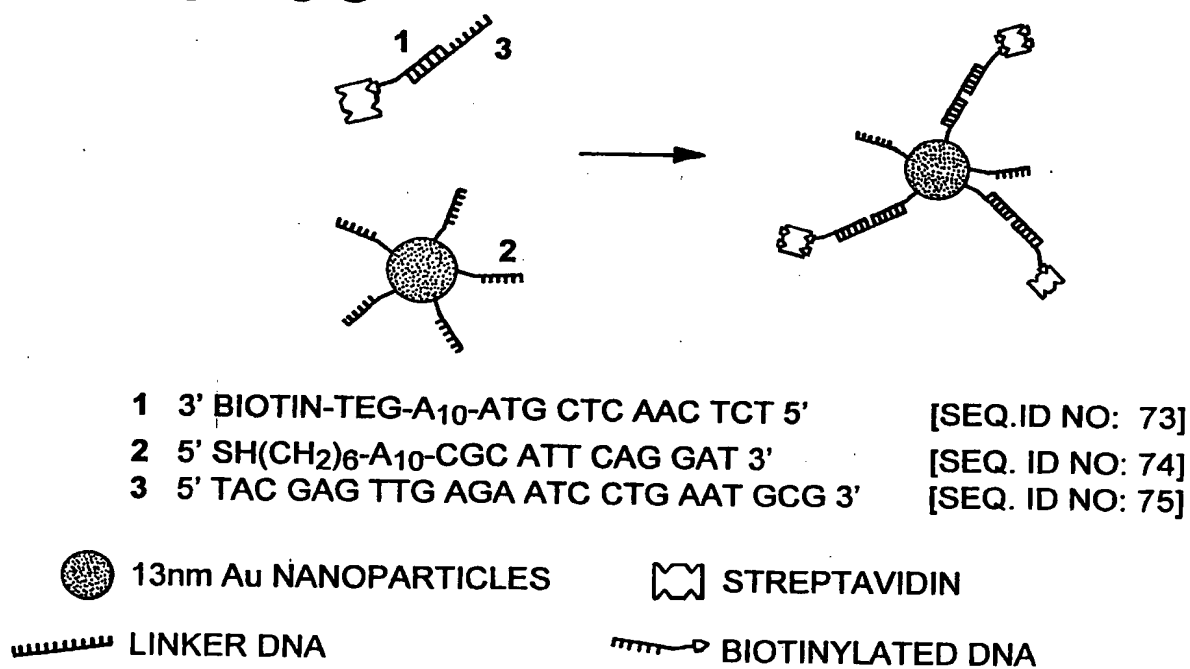


FIG. 57A

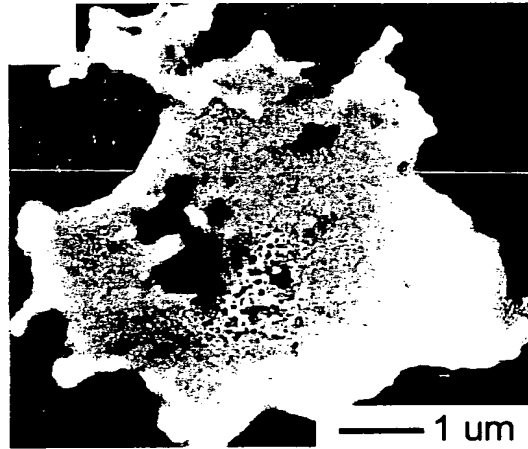


FIG. 57B

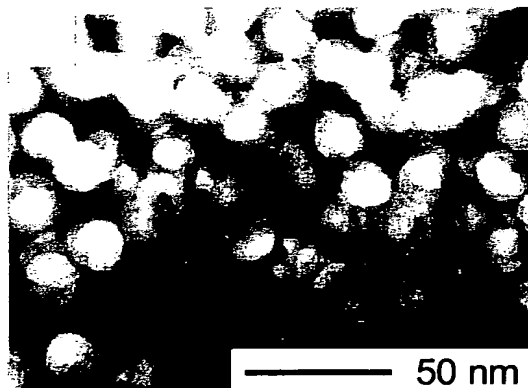


FIG. 58A

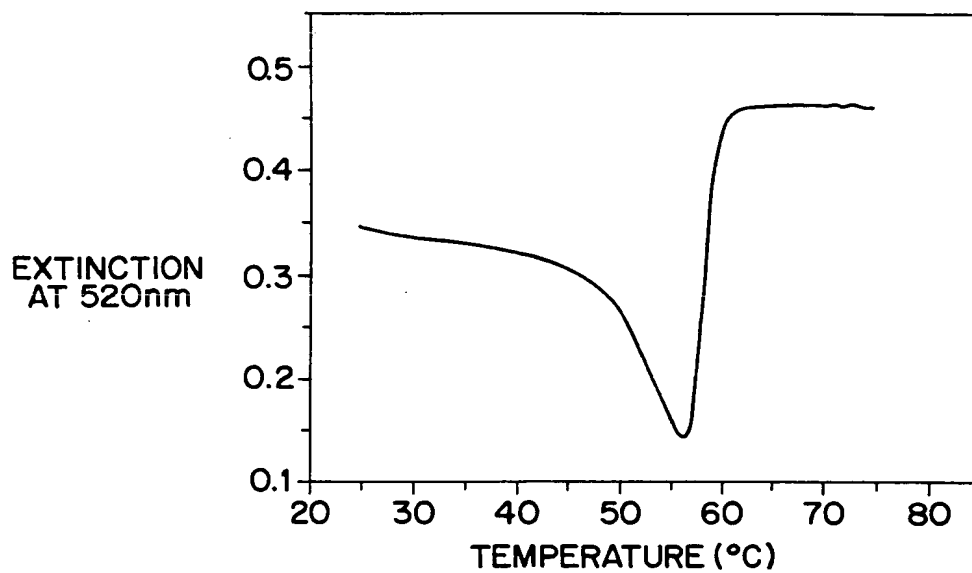


FIG. 58B

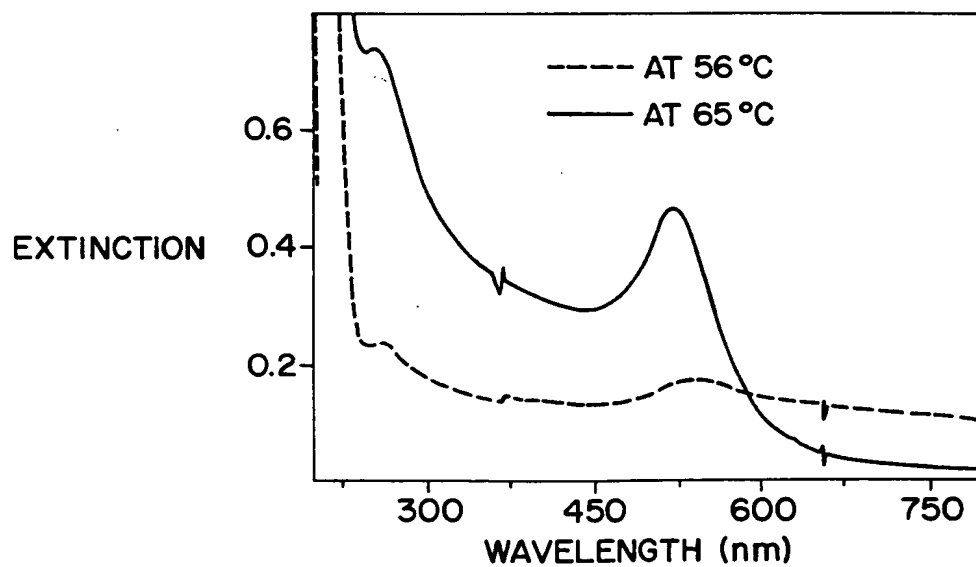


FIG. 59

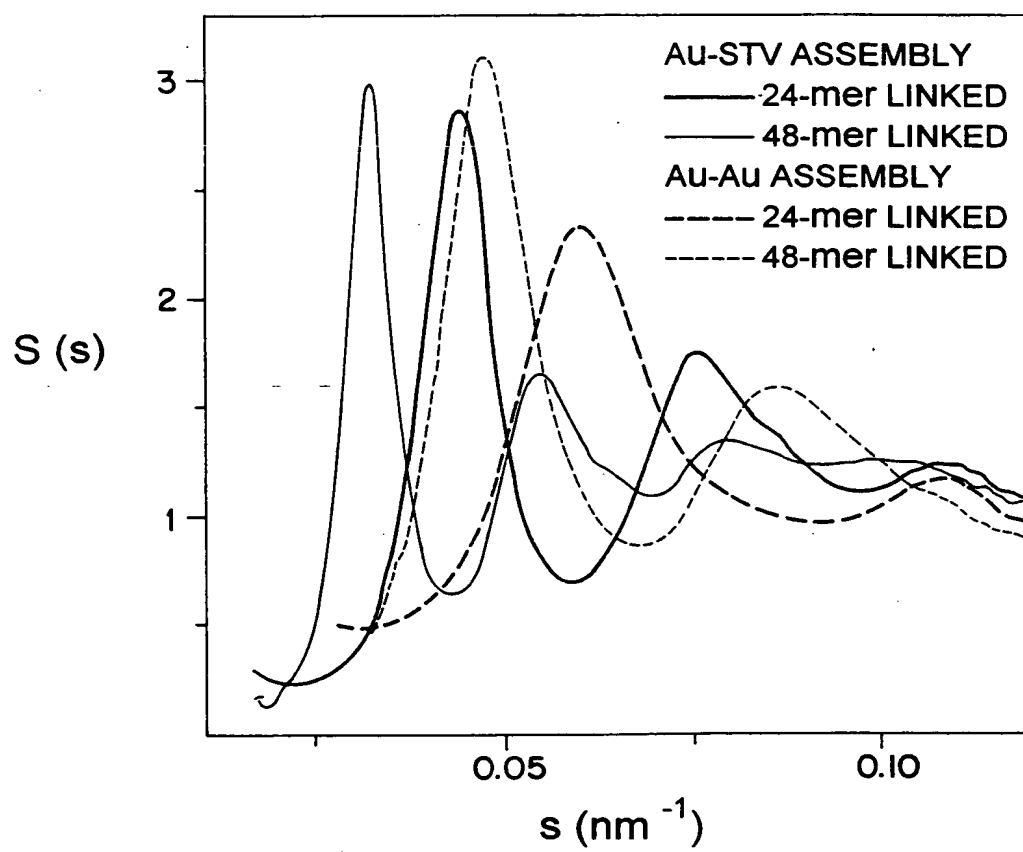


Figure 60

Scheme 1

